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Access DB# 59259

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: R GITOMER Examiner #: 69630 Date: 3/18/03
Art Unit: 1651 Phone Number 308-0732 Serial Number: 09/942,349
Mail Box and Bldg/Room Location: 1184 01 Results Format Preferred (circle): PAPER DISK E-MAIL
11 B01 11D11

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

JAN

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

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     (FILE 'HOME' ENTERED AT 06:45:38 ON 26 MAR 2003)
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     FILE 'REGISTRY' ENTERED AT 06:45:52 ON 26 MAR 2003
               E POLYETHYLENETEREPHTHALATE/CN
               E POLY(ETHYLENETEREPHTHALATE)/CN
               E POLY(ETHYLENE TEREPHTHALATE)/CN
L1             1 S E3
L2             1 S E8
L3             1 S L1,L2
               E C8H6O4/MF
L4            77 S E3 AND 46.150.18/RID
L5             4 S L4 AND 1 4 BENZENEDICARBOXYLIC
L6             1 S L5 NOT (RADICAL OR D/ELS OR 11C)
               E C8H4CL2O2/MF
L7            27 S E3 AND 46.150.18/RID
L8             1 S L7 AND 1 4 BENZENEDICARBONYL
               E ETHYLENEGLYCOL/CN
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L9             1 S E3
               E C2H4CL2/MF
L10           36 S E3
L11           12 S L10 AND 1 2 DICHLORO
               E ETHANE, 1,2-DICHLORO-/CN
L12            1 S E3
L13            2 S L6,L8
L14            2 S L9,L12
               SEL RN L13
L15        28106 S E1-E2/CRN
               SEL RN L14
L16        31985 S E3-E4/CRN
L17         9630 S L15 AND L16
L18            6 S L17 AND PMS/CI AND 2/NC
L19            3 S L18 NOT (TRIMER OR DIMER OR MAN/CI)
L20            4 S L3,L19
L21            1 S SUCROSE/CN
L22            3 S 69257-56-3 OR 92240-93-2 OR 92184-34-4
L23            1 S 56086-34-1
L24            3 S L21-L23 AND SUCROSE
L25            2 S L24 NOT ISOSUCROSE
               SEL RN
L26         1706 S E5-E6/CRN
               E TRIS(HYDROXYMETHYL)AMINOMETHANE/CN
L27            1 S E3
               SEL RN
L28          942 S E1/CRN

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L29           35 S ENGLEBRETH?(S)HOLM?(S)SWARM?
               E MEMBRANE/CT
L30        32694 S E3
               E E69+ALL
L31        32694 S E1
L32       157595 S E1+NT
L33          712 S L31,L32 (L) EXTRACELL?
               E EXTRACELLULAR MATRIX/CT
               E E3+ALL
L34        11032 S E14,E13+NT
L35           24 S L29 AND L30-L34
L36           17 S L29 AND EXTRACELL?(L) MATRIX
L37           25 S L29 AND ?MEMBRAN?
```

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L38        60050 S L20
L39        55688 S POLYETHYLENETEREPHTHAL? OR POLY()(ETHYLENETEREPHTHAL? OR ETHY
L40        45726 S PET
L41          147 S POLY OXY 1 2 ETHANEDIYLOXYCARBONYL 1 4 PHENYLENECARBONYL
L42         1059 S DIMETHYL TEREPHTHALATE ETHYLENE GLYCOL COPOLYMER
L43         5617 S MELINEX OR MYLAR OR LUMIRROR OR PA 200
L44         3741 S (ETHYLENE GLYCOL OR ETHYLENEGLYCOL)()(TEREPHTHALIC ACID OR TE
L45            1 S L29 AND L38-L44
L46            1 S L29 AND (POLYOL OR POLYHYDRIC (L) ALCOHOL)
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L50            3 S L49 AND L35-L37
                 SEL DN AN 1
L51            1 S E1-E3 AND L50
L52            1 S L29 AND COAT?/SC,SX,CW
L53            1 S L29 AND COAT?
L54            1 S L51-L53
                 E MANNUZZA F/AU
L55           10 S E4-E6
                 E FLAHERTY P/AU
L56            4 S E4,E12,E13
                 E ILLSLEY S/AU
L57            1 S E4
                 E ILSLEY S/AU
L58            4 S E3,E4
                 E KRAMER M/AU
L59          287 S E3,E16
                 E KRAMER MARTIN/AU
L60           36 S E3,E5
                 E BECTON/PA,CS
L61         1649 S (BECTON? OR DICKINSON?)/PA,CS
L62            1 S L29 AND L55-L61
L63            1 S L54,L62
L64            4 S L29 AND (BIOCHEM?(L)METHOD?)/SC,SX
L65            4 S L63,L64
L66           31 S L29 NOT L65
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L69            0 S L29 AND ?POLYM?
                 E COATING/CT
                 E E11+ALL
L70            1 S L29 AND E3,E2+NT
                 E E116+ALL
L71            1 S L29 AND E7+NT
L72            4 S L68,L70,L71
                 E SEAL/CT
                 E E21+ALL
L73            1 S L29 AND E1
                 E E8+ALL
L74            0 S L29 AND E3,E4,E2+NT
L75            4 S L72,L73

=> fil hcaplus
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FILE COVERS 1907 - 26 Mar 2003 VOL 138 ISS 13
FILE LAST UPDATED: 25 Mar 2003 (20030325/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L75 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:272858** HCAPLUS
DN **136:259554**
TI Porous **membrane** comprising an extracellular **membrane** and a **polyol**
IN **Mannuzza, Frank J.; Flaherty, Paula; Illsley, Stephen R.; Kramer, Martin L.**
PA **Becton, Dickinson and Company, USA**
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C12N005-00
CC **9-1** (**Biochemical Methods**)
Section cross-reference(s): 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1195432	A2	20020410	EP 2001-122845	20010924
	EP 1195432	A3	20020417		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 2000-235712P	P	20000927		
	US 2001-942349	A	20010829		

AB A porous **membrane** is **coated** with a compn. which includes a reconstituted and aggregated **extracellular matrix** derived from the **Englebreth-Holm-Swarm** mouse tumor, a **polyol** and a pH 7.8-8.2 **buffer**. The **coated membrane** is dried, affixed to an insert portion of an assembly and received in a well of a multiwell tissue culture plate. The invention includes a method to make the **coated membrane**.
ST porous **membrane** extracellular **polyol**
IT Neoplasm
(**Englebreth-Holm-Swarm** mouse; porous **membrane** comprising extracellular **membrane** and a **polyol**)
IT **Membrane, biological**
(**Extracellular**; porous **membrane** comprising **extracellular membrane** and a **polyol**)
IT **Alcohols**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**polyhydric**; porous **membrane** comprising extracellular **membrane** and a **polyol**)
IT Aggregation
Animal cell

Animal tissue culture
Buffers
Coating materials
Coating process
Composition
Drying
Extracellular matrix
Interface
Lids
Plates
Sealing
Solutions
Wells
pH
(porous **membrane** comprising **extracellular membrane** and a **polyol**)

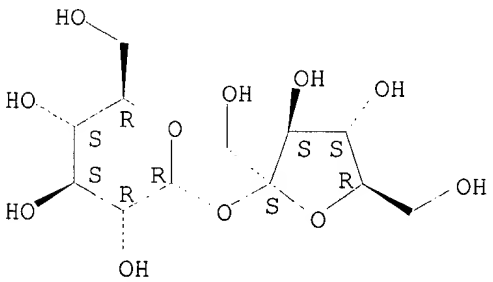
IT Polyesters, biological studies
Salts, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(porous **membrane** comprising extracellular **membrane** and a **polyol**)

IT **57-50-1, Sucrose**, biological studies **77-86-1, Tris(hydroxymethyl)aminomethane** **25038-59-9, Polyethyleneterephthalate**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(porous **membrane** comprising extracellular **membrane** and a **polyol**)

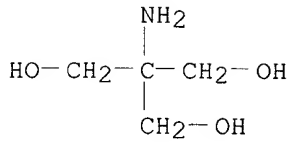
IT **57-50-1, Sucrose**, biological studies **77-86-1, Tris(hydroxymethyl)aminomethane** **25038-59-9, Polyethyleneterephthalate**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(porous **membrane** comprising extracellular **membrane** and a **polyol**)

RN 57-50-1 HCAPLUS
CN .alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl (9CI) (CA INDEX NAME)

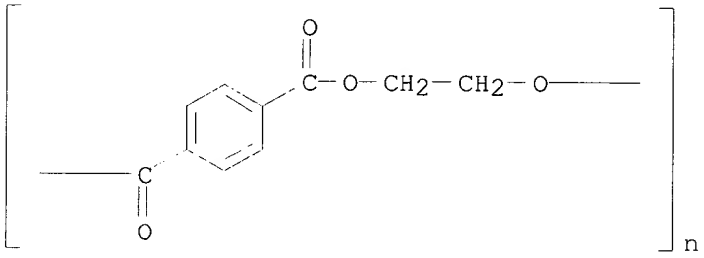
Absolute stereochemistry.



RN 77-86-1 HCAPLUS
CN 1,3-Propanediol, 2-amino-2-(hydroxymethyl)- (8CI, 9CI) (CA INDEX NAME)



RN 25038-59-9 HCAPLUS
CN Poly(oxy-1,2-ethanediyloxycarbonyl-1,4-phenylenecarbonyl) (9CI) (CA INDEX NAME)



L75 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:558823 HCAPLUS
DN 122:310179
TI Matrigel treatment of primary hepatocytes following DNA transfection enhances responsiveness to extracellular stimuli
AU Shih, Hsiu-Ming; Towle, Howard C.
CS Univ. Minnesota, Minneapolis, MN, USA
SO BioTechniques (1995), 18(5), 813-16
CODEN: BTNQDO; ISSN: 0736-6205
PB Eaton
DT Journal
LA English
CC **9-11** (**Biochemical Methods**)
Section cross-reference(s): 13
AB When hepatocytes were cultured on Matrigel (a reconstituted gel matrix derived from the **Englebreth-Holm-Swarm** mouse sarcoma tumor), the cells showed enhanced responsiveness to growth or thyroid hormones, and cell stimulation could be maintained for at least 5 days, compared to cells cultured directly on plastic.
ST hepatocyte culture Matrigel DNA transfection
IT Animal tissue culture
Extracellular matrix
Transformation, genetic
(Matrigel treatment of primary hepatocytes following DNA transfection enhances responsiveness to extracellular stimuli)
IT Liver
(hepatocyte, Matrigel treatment of primary hepatocytes following DNA transfection enhances responsiveness to extracellular stimuli)
IT 119978-18-6, Matrigel
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Matrigel treatment of primary hepatocytes following DNA transfection enhances responsiveness to extracellular stimuli)

L75 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 1991:38736 HCAPLUS
DN 114:38736
TI Effects of extracellular matrix on the expression of specific ovarian

proteins
AU Maresh, Grace A.; Timmons, Therese M.; Dunbar, Bonnie S.
CS Dep. Cell Biol., Baylor Coll. Med., Houston, TX, 77030, USA
SO Biology of Reproduction (1990), 43(6), 965-76
CODEN: BIREBV; ISSN: 0006-3363
DT Journal
LA English
CC **9-11** (**Biochemical Methods**)
Section cross-reference(s): 13
AB A unique ovarian follicle cell culture system has been established to analyze the effects of extracellular matrix (ECM) on early granulosa cell differentiation. Primary and early secondary follicles isolated from ovaries of sexually immature rabbits were grown on poly-D-lysine or **Englebreth-Holm-Swarm** basement membrane biomatrix substrata (EHS) in serum-free, hormonally defined medium. Granulosa cells from these follicles were examd. for growth pattern characteristics and for secretory protein synthesis by 2-dimensional (2D) PAGE. Whereas some proteins were synthesized by cells on either matrix, the expression of other secreted proteins was markedly affected by the ECM used. Secretion of zona pellucida (ZP) proteins was demonstrated by ELISA assays and immunoblots of 1-dimensional (1D) and 2D-PAGE sepns. of secreted proteins probed with monoclonal and epitope-selected antibodies. Expression of 2 ZP proteins was altered by ECM: 55-kDa endo-.beta.-galactosidase (EBGD)-treated ZP glycoprotein (55-kDaEBGD) was secreted by cells grown on either ECM, but a greater amt. of 75-kDaEBGD was secreted by cells grown on poly-D-lysine. Thus, granulosa cells from early-stage follicles express ZP proteins in vitro in the absence of oocytes, although proper post-translational modification may not occur. Also, the ECM has a dramatic effect on the expression of secretory proteins.
ST granulosa cell culture extracellular matrix; zona pellucida protein ovary culture
IT Extracellular matrix
(Matrigel or poly-D-lysine as, for ovary follicle culture)
IT Animal tissue culture
(of ovary follicles and granulosa cell, zona pellucida protein formation in)
IT Glycoproteins, biological studies
RL: BIOL (Biological study)
(of zona pellucida, expression of, by ovary granulosa cells in culture, extracellular matrix effect on)
IT Ovary, metabolism
(follicle cell, ovary-specific protein formation by, in culture, extracellular matrix effect on)
IT Egg
(zona pellucida, glycoproteins of, expression of, by granulosa cells in culture, extracellular matrix effect on)
IT 26853-89-4, Poly-D-lysine 26913-90-6, Poly-D-lysine 119978-18-6, Matrigel
RL: ANST (Analytical study)
(as extracellular matrix, ovary granulosa cell culture on, zona pellucida proteins in)

L75 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 1989:403650 HCAPLUS
DN 111:3650
TI Immunohistochemical localization of materials reacting with antibody to glomerular proteoglycans
AU Makino, Hirofumi; Kumagai, Isao; Ikeda, Shuji; Kashihara, Naoki; Hirakawa, Shuzo; Ota, Zensuke
CS Med. Sch., Okayama Univ., Okayama, Japan
SO Ketsugo Soshiki (1988), 20(2), 65-70
CODEN: KESOD3; ISSN: 0389-7079

DT Journal
LA English
CC **9-10 (Biochemical Methods)**
Section cross-reference(s): 13, 14, 15
AB Heparan sulfate proteoglycans (HS-PGs) were purified from rat glomeruli and a specific polyclonal antibody to HS-PGs was raised. The localization of materials showing cross-reactivity to this antibody was studied in various rat tissues by an indirect immunofluorescence method. The basement membranes of the glomeruli, urinary tubules, and Bowman's capsule reacted linearly with the antibody. The antibody reacted with the basement membrane matrixes of cornea, lens, alveoli, intestinal epithelium, transitional cells of the urinary bladder, and testicular seminiferous tubules. The capillary walls in cerebral cortex were also reactive. An intensely pos. reaction was also obsd. in the cytoplasm of PYS-2 cells and the extracellular matrixes of **Englebreth-Holm-Swarm** sarcoma which is known to be the basement membrane-producing tumor. However, the antibody did not react with the cell surfaces of various epithelial cells tested. This antibody will be a useful tool for studying the immunohistochem. localization of basement membrane-assocd. HS-PGs.
ST basement membrane heparan sulfate proteoglycan antibody
IT Capillary vessel
(of brain cortex, basement membrane of, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)
IT Basement membrane
(proteoglycans assocd. with, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan in immunohistochem. localization of)
IT Antibodies
RL: ANST (Analytical study)
(to heparan sulfate-contg. glomerular proteoglycan, in immunohistochem. localization of basement membrane-assocd. proteoglycans)
IT Animal cell line
(EHS, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)
IT Lung, composition
(alveolus, basement membrane of, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)
IT Brain, composition
(cerebral cortex, basement membrane of capillaries of, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)
IT Eye, composition
(cornea, basement membrane of, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)
IT Intestine, composition
(epithelium, basement membrane of, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)
IT Kidney, composition
(glomerulus, heparan sulfate-contg. proteoglycan of, polyclonal antibody to, in immunohistochem. localization of basement membrane-assocd. proteoglycans)
IT Immunochemical analysis
(immunofluorescent staining, for proteoglycans assocd. with basement membrane)
IT Eye, composition
(lens, basement membrane of, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)
IT Bladder
(neoplasm, basement membrane of, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)
IT Mucopolysaccharides, biological studies
RL: BIOL (Biological study)
(proteoglycans, heparitin sulfate-contg., polyclonal antibody to

glomerular, in immunohistochem. localization of basement membrane-assocd. proteoglycans)
IT Testis, composition
(seminiferous tubule, basement membrane of, polyclonal antibody to heparan sulfate-contg. glomerular proteoglycan staining of)

=> s l29 not l75
L76 31 L29 NOT L75

=> s l76 and l29-l75
L77 31 L76 AND (L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR L42 OR L43 OR L44 OR L45 OR L46 OR L47 OR L48 OR L49 OR L50 OR L51 OR L52 OR L53 OR L54 OR L55 OR L56 OR L57 OR L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR L66 OR L67 OR L68 OR L69 OR L70 OR L71 OR L72 OR L73 OR L74 OR L75)

=> d bib abs hitstr retable tot

L77 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 2003:155327 HCAPLUS
TI Altered morphology in cultured rat intestinal epithelial IEC-6 cells is associated with alkaline phosphatase expression
AU Wood, S. R.; Zhao, Q.; Smith, L. H.; Daniels, C. K.
CS College of Pharmacy, Department of Pharmaceutical Sciences, Idaho State University, Box 8334, Pocatello, ID, 83209, USA
SO Tissue & Cell (2003), 35(1), 47-58
CODEN: TICEBI; ISSN: 0040-8166
PB Elsevier Science Ltd.
DT Journal
LA English
AB Non-transformed, rat intestinal epithelial cells (IEC-6), and human intestinal colonic carcinoma cells (CACO-2) have both been used to study processes of epithelial cell differentiation. However, only CACO-2 cells have been described as spontaneously expressing phenotypic changes of differentiation in culture. We report here that when IEC-6 cells are grown in post-confluent culture, they develop structural changes similar to those seen in cells induced to differentiate by culture on **Englebreth-Holm-Swarm** (EHS) **extracellular matrix** proteins. Correlated with this morphol. change is loss of nuclear localization of c-myc protein and development of cell surface alk. phosphatase (ALP) enzymic activity. MRNAs for liver and intestinal isoforms of ALP were expressed in both pre- and post-confluent cells. Inhibition of ALP activity in post-confluent cells by levamisole indicated the expressed ALP activity to be of the liver isoform. We suggest the expression of ALP activity, which occurs concomitantly with morphol. alterations in post-confluent IEC-6 cells, represents increased expression and localization to the cell surface of the liver isoform of ALP. Cultured IEC-6 cells may provide a non-transformed, in vitro alternative to CACO-2 cells for study of epithelial cell differentiation.

L77 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:681278 HCAPLUS
DN 130:79696
TI Dedifferentiation of human hepatocytes by **extracellular matrix** proteins in vitro: quantitative and qualitative investigation of cytokeratin 7, 8, 18, 19 and vimentin filaments
AU Blaheta, Roman A.; Kronenberger, Bernd; Woitaschek, Dirk; Auth, Marcus K. H.; Scholz, Martin; Weber, Stephan; Schuldes, Horst; Encke, Albrecht; Markus, Bernd H.
CS Department of General Surgery, Hospital of the Johann Wolfgang

Goethe-University, Frankfurt am Main, 60590, Germany
SO Journal of Hepatology (1998), 28(4), 677-690
CODEN: JOHEEC; ISSN: 0168-8278
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB Liver cirrhosis and carcinogenesis are accompanied by an alteration in **extracellular matrix** material. Histol. studies reveal upregulation of the intermediate filaments cytokeratins 8 and 18 and de novo synthesis of vimentin, and cytokeratin 7 or 19 in hepatocytes. The aim of this study was to investigate how these two processes are linked. Human hepatocytes were seeded: (i) on the **matrix** components collagen I, IV, laminin, or fibronectin; (ii) on stoichiometrically different complete **matrixes**, derived from human placenta (**matrix** I) or the **Englebreth-Holm-Swarm** tumor (**matrix** II), and (iii) inside a three-dimensional collagen I sandwich. Filament expression and assembly were measured by cytofluor anal. or confocal laserscan microscopy. The **matrix** components or complete **matrixes** triggered enhancement of cytokeratins 8 and 18 and de novo synthesis of cytokeratins 7, 19 and vimentin in a characteristic way. Confocal images demonstrated a dense and uniform network of cytokeratin 18 in freshly isolated cells, which was "replaced" by a few, thick protein bundles within 20 days. Interestingly, newly synthesized cytokeratin 19 structurally resembled the cytokeratin 19 organization in biliary epithelial cells. Marked cytokeratin alterations could be partially prevented when hepatocytes were grown in a three-dimensional collagen sandwich. Pathol. alterations to the chem. compn., mol. structure, or spatial arrangement of the liver **matrix** lead to specific changes in the intermediate filament pattern in human hepatocytes. We assume that degrdn. of the **matrix** results in pathol. alterations to the hepatocyte-receptor **matrix**-ligand ratio, followed by a switch from physiol. to pathol. cell-activation.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Arterburn, L	1995	21	175	Hepatology	
Arthur, M	1994	190	825	Path Res Pract	HCAPLUS
Auth, M	1993	18	546	Hepatology	MEDLINE
Baffet, G	1991	99	609	J Cell Sci	
Ben-Ze'Ev, A	1988	85	2161	Proc Natl Acad Sci U	HCAPLUS
Bissell, D	1988	23	1	Scand J Gastroentero	
Blaheta, R				J Immunol Methods:in	
Carroll, K	1988	254	G355	Am J Physiol	MEDLINE
Chenery, R	1987	15	312	Drug Metabol Dispos	HCAPLUS
Chojkier, M	1988	8	808	Hepatology	HCAPLUS
Christensen, L	1992	100	6	APMIS	
Clement, B	1984	4	373	Hepatology	MEDLINE
Clement, B	1988	8	794	Hepatology	MEDLINE
Dipersio, C	1991	11	4405	Mol Cell Biol	HCAPLUS
Dunn, J	1991	7	237	Biotechnol Prog	HCAPLUS
Franke, W	1981	134	345	Exp Cell Res	HCAPLUS
Grant, M	1987	36	2311	Biochem Pharmacol	HCAPLUS
Guillouzo, A	1985	34	2991	Biochem Pharmacol	HCAPLUS
Ismail, T	1991	14	1076	Hepatology	HCAPLUS
Kato, S	1992	198	59	Exp Cell Res	HCAPLUS
Keppens, S	1993	17	610	Hepatology	HCAPLUS
Kleinman, H	1986	25	312	Biochemistry	HCAPLUS
Koivunen, E	1991	51	2107	Cancer Res	HCAPLUS
Lai, Y	1989	113	134	Arch Pathol Lab Med	MEDLINE
Li, M	1987	84	136	Proc Natl Acad Sci U	HCAPLUS
Lichtinghagen, R	1995	33	65	Eur J Clin Chem Clin	HCAPLUS
Liotta, L	1986	55	1037	Ann Rev Biochem	HCAPLUS

Marceau, N	1983	29	421	Cell Mol Biol	HCAPLUS
Martinez-Hernandez, A	1991	64	157	Lab Invest	HCAPLUS
McGuire, R	1992	15	989	Hepatology	MEDLINE
Michalopoulos, G	1993	156	443	J Cell Physiol	HCAPLUS
Moll, R	1982	31	11	Cell	HCAPLUS
Moll, R	1991	65	74	Lab Invest	HCAPLUS
Mooney, D	1992	151	497	J Cell Physiol	HCAPLUS
Neubauer, K	1995	108	1124	Gastroenterology	HCAPLUS
Orkin, R	1977	145	204	J Exp Med	HCAPLUS
Rana, B	1994	14	5858	Mol Cell Biol	HCAPLUS
Reid, L	1992	15	1198	Hepatology	MEDLINE
Richard, B	1990	41	255	Biochem Pharmacol	
Robinson, J	1984	98	946	J Cell Biol	HCAPLUS
Ryan, C	1993	113	48	Surgery	MEDLINE
Santhosh, A	1994	137	127	Mol Cell Biochem	HCAPLUS
Sawada, N	1986	167	458	Exp Cell Res	HCAPLUS
Schroder, A	1995	59	1023	Transplantation	MEDLINE
Schroder, A	1994	119	127	Zentralbl Chir	MEDLINE
Schuetz, E	1988	134	309	J Cell Physiol	HCAPLUS
Shirahase, I	1995	5	77	Eur J Pediatr Surg	MEDLINE
Springer, T	1990	346	425	Nature	HCAPLUS
Strain, A	1994	210	1	Exp Cell Res	
Sudhakaran, P	1986	167	505	Exp Cell Res	HCAPLUS
Takahara, T	1995	21	787	Hepatology	HCAPLUS
Terada, T	1995	26	746	Hum Pathol	MEDLINE
Teti, A	1992	2	83	J Am Soc Nephrol	
Tryggvason, K	1987	907	191	Biochim Biophys Acta	HCAPLUS
van Eyken, P	1988	19	562	Hum Pathol	MEDLINE
Yong, K	1990	4	211	Blood Rev	MEDLINE

L77 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:403265 HCAPLUS
DN 129:134210
TI Differential localization of laminin chains in bovine follicles
AU Van Wezel, I. L.; Rodgers, H. F.; Rodgers, R. J.
CS Dep. Med., Flinders University of South Australia, Bedford Park, 5042, Australia
SO Journal of Reproduction and Fertility (1998), 112(2), 267-278
CODEN: JRPFA4; ISSN: 0022-4251
PB Journals of Reproduction and Fertility Ltd.
DT Journal
LA English
AB The compn. of a basal lamina markedly affects its ability to filter material and affects the fate of adjacent epithelial cells. Therefore, basal laminae differ in compn. with tissue development, and between different tissues in the body. Laminins are a component of basal laminae and consist of 1 .alpha., 1 .beta., and 1 .gamma. chain, of which there are at least 5, 3, and 2 isoforms, resp. This is the 1st study to immunolocalize a range of these individual laminin chains (.alpha.1, .alpha.2, .beta.1, .beta.2, .gamma.1) in ovarian follicles. Frozen sections of bovine ovaries (n = 6) were immunostained using specific antisera to laminin chains and factor VIII-related antigen (to identify endothelial cells). Secondary antisera were labeled with 1 of 2 different fluorochromes (DTAF and Cy3), and dual localization of laminin chains and factor VIII-related antigen was performed. The .alpha.1, .beta.2, and .gamma.1 chains were consistently localized to the follicular basal lamina in all healthy follicles. Staining was less intense in the atretic antral follicles. Conversely, .alpha.2 and .beta.1 were rarely present in the follicular basal laminae of healthy antral follicles. Two of 9 healthy antral follicles obsd. stained weakly for .alpha.2 in their basal lamina, and .beta.1 was present at low concns. in growing preantral follicles. In atretic antral follicles, the follicular basal lamina stained pos. for .alpha.1, .alpha.2, and .beta.2, but no .beta.1 was detected, and the

.gamma.1 staining was less intense than in healthy follicles. Antisera to **Englebreth Holm-Swarm** tumor laminin stained basal laminae of all follicles. In the theca of antral follicles, .beta.1 and .beta.2 chains were both present in the vasculature. Staining for the .gamma.1 chain was present in the thecal vasculature and generally throughout the theca of healthy and atretic antral follicles. Therefore, the compn. of the follicular basal lamina alters during development and atresia, and potentially plays a role in the changing identity of the granulosa cells and the accumulation of antral follicular fluid.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Amsterdam, A	1989	124	1956	Endocrinology	HCAPLUS
Amsterdam, A	1975	67	894	Journal of Cell Biol	HCAPLUS
Andersen, M	1976	48	109	Journal of Reproduct	HCAPLUS
Bagavandoss, P	1983	31	633	Journal of Histochem	MEDLINE
Bortolussi, M	1977	183	329	Cell and Tissue Rese	HCAPLUS
Burgeson, R	1994	14	209	Matrix Biology	HCAPLUS
Christiane, Y	1988	50	48	Fertility and Steril	HCAPLUS
Durbeej, M	1997	15	397	Matrix Biology	
Ehrig, K	1990	87	3264	Proceedings of the N	HCAPLUS
Ekblom, P	1989	3	2141	FASEB Journal	HCAPLUS
Engvall, E	1993	43	2	Kidney International	HCAPLUS
Faddy, M	1995	10	770	Human Reproduction	MEDLINE
Figueiredo, J	1995	43	845	Theriogenology	HCAPLUS
Frojdman, K	1992	50	113	Differentiation	MEDLINE
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Frojdman, K	1992	97	469	Histochemistry	HCAPLUS
Frojdman, K	1989	33	99	International Journa	MEDLINE
Frojdman, K	1995	39	335	International Journa	HCAPLUS
Gosden, R	1988	82	813	Journal of Reproduct	MEDLINE
Greenwald, G	1988		387	The Physiology of Re	
Hay, E	1991			Cell Biology of Extr	
Hunter, D	1989	338	229	Nature	HCAPLUS
Iivanainen, A	1995	365	183	FEBS Letters	HCAPLUS
Kaneko, Y	1984	36	2473	Acta Obstetrica et G	
Klein, G	1988	55	331	Cell	HCAPLUS
Klein, G	1990	110	823	Development	HCAPLUS
Leardkamolkarn, V	1992	233	41	Anatomical Record	MEDLINE
Leivo, I	1989	60	426	Laboratory Investiga	
Leivo, I	1989	61	426	Laboratory Investiga	MEDLINE
Leivo, I	1988	85	1544	Proceedings of the N	HCAPLUS
Leu, F	1986	34	483	Journal of Histochem	MEDLINE
Lindblom, A	1994	219	383	European Journal of	HCAPLUS
Luck, M	1994	16	33	Oxford Reviews in Re	
Noakes, P	1995	10	400	Nature Genetics	MEDLINE
O'Shea, J	1978	187	473	Cell and Tissue Rese	
Palotie, A	1984	4	279	Collagen Related Res	HCAPLUS
Paulsson, M	1992	27	93	Critical Reviews in	HCAPLUS
Paulsson, M	1989	264	18726	Journal of Biologica	HCAPLUS
Perreault, N	1995	242	242	Anatomical Record	HCAPLUS
Rajakoski, E	1960	52	6	Acta Endocrinologica	
Richardson, M	1992	7	12	Human Reproduction	MEDLINE
Rodgers, H	1995	282	463	Cell and Tissue Rese	MEDLINE
Rodgers, R	1986	78	627	Journal of Reproduct	HCAPLUS
Sanes, J	1983	48	667	Cold Spring Harbor S	
Schuger, L	1996	179	264	Developmental Biolog	HCAPLUS
Smith, C	1991	174	171	Journal of Anatomy	MEDLINE
Timpl, R	1986	29	1	International Review	HCAPLUS
Timpl, R	1994	14	275	Matrix Biology	HCAPLUS
van Wezel, I	1996	55	1003	Biology of Reproduct	HCAPLUS
Walker-Caprioglio, H	1995	281	187	Cell and Tissue Rese	MEDLINE

Watt, F	1986	11	482	Trends in Biochemica	HCAPLUS
Wordinger, R	1983	228	141	Journal of Experimen	HCAPLUS
Yoshimura, Y	1991	62	529	Animal Science and T	
Yoshinaga-Hirabayashi,	1990	93	223	Histochemistry	HCAPLUS
Yurchenco, P	1990	4	1577	FASEB Journal	HCAPLUS
Zhao, Y	1995	104	115	Journal of Reproduct	HCAPLUS
Zhou, J	1994	269	13193	Journal of Biologica	HCAPLUS
Zlotkin, T	1986	119	2809	Endocrinology	HCAPLUS
Zoller, L	1978	103	310	Endocrinology	HCAPLUS
Zoller, L	1979	62	125	Histochemistry	HCAPLUS

L77 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:472438 HCAPLUS
DN 125:163947
TI Carboxy terminal sequence and synthesis of rat kidney laminin .gamma.1 chain
AU Vanden Heuvel, Gregory B.; Leardkamolkarn, Vijittra; St. John, Patricia L.; Abrahamson, Dale R.
CS School Medicine, Yale University, New Haven, CT, USA
SO Kidney International (1996), 49(3), 752-760
CODEN: KDYIA5; ISSN: 0085-2538
PB Blackwell
DT Journal
LA English
AB We used antibodies against mouse **Englebreth-Holm-Swarm** (EHS) tumor laminin to screen a newborn rat kidney .lambda.gt11 expression library and isolated three overlapping cDNA clones, termed 2b-11 (401 bp), 10-b7 (779 bp), and 2a (2,095 bp). DNA sequence anal. identified these cDNAs as encoding much of the carboxy terminal domain I/II of laminin .gamma.1 chain (formerly referred to as B2e), and 1436 bp of the 3' untranslated region. In situ hybridization of fetal (E15) rat sections localized laminin .gamma.1 chain mRNA primarily to meninges of the brain, auditory and peripheral nerve fibers, gastrointestinal system, and developing lung airway epithelium. Intense hybridization was also found in early nephric structures and glomeruli of fetal kidneys. In kidneys of three-day-old rats, hybridization persisted over early nephric figures, developing glomeruli, and collecting ducts, but considerably less hybridization was seen over tubules. On Northern blots of neonatal kidney RNA, the three cDNA clones hybridized to two species of 7.5 and 5.5 kb, suggesting that developing rat kidney laminin .gamma.1 mRNAs are processed using two different polyadenylation signals.

L77 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:470701 HCAPLUS
DN 125:164120
TI Human SY5Y neuroblastoma cell interactions with laminin isoforms: Neurite outgrowth on laminin-5 is mediated by integrin .alpha.3.beta.1
AU Smith, Barbara E.; Bradshaw, Amy D.; Choi, Esther S. H.; Rouselle, Patricia; Wayner, Elizabeth A.; Clegg, Dennis O.
CS Neuroscience Research Institute, University California, Santa Barbara, CA, 93106, USA
SO Cell Adhesion and Communication (1996), 3(6), 451-462
CODEN: CADCEF; ISSN: 1061-5385
PB Harwood
DT Journal
LA English
AB Laminin (Ln) isoforms may play important roles in neuronal development, particularly axon guidance, but neural receptors mediating interactions with Ln are not entirely understood. This paper describes compared the adhesive and process outgrowth activities of a human neuroblastoma cell line SY5Y on various laminin isoforms. Cell adhesion and process outgrowth were examd. on murine Ln-1 (**Englebreth-Holm-Swarm** sarcoma laminin), human placental Ln-1 (human Ln-1[p]),

human Ln-2 (merosin), human Ln-5 (kalinin/epiligrin/nicein), and human foreskin keratinocyte **extracellular matrix** ext. (human HFK-ECM). Ln-5 was shown to evoke process outgrowth in amts. comparable to other Ln isoforms. Antibody perturbation expts. showed that adhesion and process outgrowth on murine Ln-1 was primarily mediated by the integrin .alpha.1.beta.1, whereas adhesion and outgrowth on human Ln-5 and human HFK-ECM were mediated by .alpha.3.beta.1. Adhesion to human Ln-1(p) and Ln-2 was not blocked by addn. of anti-.alpha.1 or anti-.alpha.3 antibodies alone, but adhesion was partially perturbed when these antibodies were added in combination. Process outgrowth on human Ln-1(p) was blocked when either anti-.alpha.3 or anti-.beta.1 antibodies were added, indicating that .alpha.3.beta.1 is the primary integrin heterodimer responsible for process extension on this substrate. These results demonstrate that Ln-5 and other Ln isoforms support comparable levels of adhesion and process outgrowth, but different integrin heterodimers, alone and in combination, are used by SY5Y cells to mediate responses.

L77 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:713187 HCAPLUS
DN 123:108734
TI Mesenchymal cell chondrogenesis is stimulated by basement **membrane** matrix and inhibited by age-associated factors
AU Bradham, Douglass M.; Passaniti, Antonino; Horton, Walter E., Jr.
CS Lab. Biol. Chem., National Inst. Health, Baltimore, MD, USA
SO Matrix Biology (1995), 14(7), 561-71
CODEN: MTBOEC; ISSN: 0945-053X
PB Fischer
DT Journal
LA English
AB During development of the embryonic limb, differentiation of mesenchymal progenitor cells into chondrocytes is regulated by cell shape, **extracellular matrix**, and growth and differentiation factors. In this study, reconstituted basement **membrane** (Matrigel) prepd. from mouse **Englebreth-Holm-Swarm** tumor tissue was found to stimulate mesenchymal cell chondrogenesis in vitro and the prodn. of cartilage at ectopic sites in athymic mice. The rate of chondrogenesis of mesenchymal cells from chick limb bud was increased four-fold by the addn. of 400 .mu.g/mL Matrigel to the media of micromass cultures, and this activity was not blocked by neutralizing antibodies to transforming growth factor-.beta. (TGF-.beta.) or fibroblast growth factor (FGF). Mesenchymal cells cultured on Matrigel, but not laminin or collagen type I or IV, formed spheres of condensed cells which stained with Alcian blue. Chick limb-bud mesenchymal cells suspended in Matrigel prepd. from tumors grown in C57 mice aged 3, 12, or 26 mo formed disks of hyaline cartilage within 2 wk with wet wts. of 59.1 mg, 35.7 mg, and 21.4 mg, indicating that the Matrigel from the old animals was less biol. active. In agreement with the in vivo data, Alcian blue staining of proteoglycan was over two-fold higher in micromass cultures supplemented with the Matrigel from young animals than in cultures treated with the Matrigel from old mice. A high-salt wash prepn. of Matrigel from tumors grown in old mice increased the rate of chondrogenesis and cartilage prodn., suggesting that an inhibitor of chondrogenesis is produced by the old host. Thus, Matrigel contains chondrogenic activity distinct from TGF-.beta. or FGF. The aged host may produce factors that are inhibitory to mesenchymal cell differentiation and adversely affect cartilage formation and repair.

L77 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:499669 HCAPLUS
DN 122:236204
TI Secreted products and **extracellular matrix** from testicular peritubular myoid cells influence androgen-binding protein secretion by Sertoli cells in culture

AU Thompson, Erik W.; Blackshaw, Alan W.; Raychoudhury, Samir S.
CS Division of Science and Technology, Griffith University, Brisbane, 4111, Australia
SO Journal of Andrology (1995), 16(1), 28-35
CODEN: JOAND3; ISSN: 0196-3635
DT Journal
LA English
AB Metabolic cooperation mediated by secreted factors between Sertoli cells and peritubular myoid cells has been well documented. The authors have confirmed that factors secreted by peritubular myoid cells modulate androgen-binding protein (ABP) secretion by Sertoli cells and shown further that this can also be achieved with peritubular myoid cell **extracellular matrix** (ECM). While peritubular myoid cell ECM potentiated the stimulatory effect of dibutyryl cAMP on Sertoli cell ABP secretion, secreted factors did not, suggesting that the two components influence Sertoli cells through distinct mechanisms. The authors also tested other factors and other cell lines for effects on ABP prodn. by Sertoli cells. The addn. of human plasma fibronectin or conditioned medium from the basement **membrane**-producing **Englebreth-Holm-Swarm** sarcoma also stimulated ABP secretion by Sertoli cells. Cocultures of epithelial Sertoli cells with the cells of mesenchymal origin, such as testicular peritubular myoid cells, embryonic skin fibroblasts, and bladder smooth muscle cells, significantly stimulated ABP secretion by Sertoli cells, but coculture with the epithelial-derived Martin-Darby canine kidney cell line had no effect on Sertoli cell-secreted ABP levels. The data further define the epithelial-mesenchymal cell interaction that exists between Sertoli cells and peritubular myoid cells in the mammalian testis.

L77 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:290435 HCAPLUS
DN 122:77418
TI Intracellular distribution of lysozyme in rat alveolar type II epithelial cells
AU Gibson, K. F.; Phadke, S.
CS School Medicine, University Pittsburgh, Pittsburgh, PA, 15261, USA
SO Experimental Lung Research (1994), 20(6), 595-611
CODEN: EXLRDA; ISSN: 0190-2148
DT Journal
LA English
AB This study investigated the intracellular distribution of lysozyme, a protein that is synthesized and secreted by rat alveolar type II epithelial (ATII) cells and alveolar macrophages, using a polyclonal antibody generated against purified rat lysozyme. Lysozyme was immunopptd. with this antibody from Triton X-100 lysates of ATII cells cultured on a basement **membrane** derived from **Englebreth -Holme-Swarm** mouse sarcoma (EHS) and radiolabeled with 35S-methionine. ATII cells cultured on EHS basement **membrane** for several days were fixed and labeled with antibodies to surfactant apoprotein A (SP-A) and lgp-120 (a lysosomal glycoprotein), or lysozyme and lgp-120, and studied by confocal microscopy. Organelles were identified that stained pos. for either anti-lysozyme or anti-lgp-120; a 2nd population of organelles contained both markers. Similarly, 2 populations of SP-A-contg. organelles were identified; 1 contained the lysosomal glycoprotein lgp-120. In addn., confocal images demonstrated that both SP-A and lysozyme were secreted by ATII cells, as evidenced by the accumulation of secretory products within the lumen of the cyst-like aggregates. When the subcellular localization of SP-A and lysozyme was studied by anal. cell fractionation, 2 populations of organelles were identified that contained SP-A or lysozyme. The lighter population accounted for .apprx.32% of SP-A and 33% of total intracellular lysozyme and was recovered in the same region of the gradient as secretory lamellar bodies. The more dense population co-localized with lysosomes and

accounted for .apprx.67% of both SP-A and lysozyme recovered. Western blots of cell fractions revealed intact lysozyme in all the cell fractions. The results of these expts. suggest that lysozyme has a similar intracellular distribution as surfactant apoprotein A in ATII cells. Lysozyme is found in fractions contg. lamellar bodies where it is packaged for secretion, and in lysosomal fractions where it may undergo degrdn.

L77 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:576077 HCAPLUS
DN 121:176077
TI Cell-**extracellular matrix** interactions can regulate the switch between growth and differentiation in rat hepatocytes: reciprocal expression of C/EBP.alpha. and immediate-early growth response transcription factors
AU Rana, Basabi; Mischoulon, David; Xie, Yuhong; Bucher, Nancy L. R.; Farmer, Stephen R.
CS Depts. of Biochemistry, Boston University School of Medicine, Boston, MA, 02118, USA
SO Molecular and Cellular Biology (1994), 14(9), 5858-69
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB Previous investigations have shown that culture of freshly isolated hepatocytes under conventional conditions, i.e., on dried rat tail collagen in the presence of growth factors, facilitates cell growth but also causes an extensive down-regulation of most liver-specific functions. This dedifferentiation process can be prevented if the cells are cultured on a reconstituted basement **membrane** gel **matrix** derived from the **Englebreth-Holm-Swarm** mouse sarcoma tumor (EHS gel). To gain insight into the mechanisms regulating this response to **extracellular matrix**, the activities of two families of transcription factors, C/EBP and AP-1, which control the transcription of hepatic and growth-responsive genes, resp., were analyzed. It was demonstrated that isolation of hepatocytes from the normal quiescent rat liver by collagenase perfusion activates the immediate-early growth response program, as indicated by increased expression of c-jun, junB, c-fos, and c-myc mRNAs. Adhesion of these activated cells to dried rat tail collagen augments the elevated levels of these mRNAs for the initial 1 to 2 h postplating; junB and c-myc mRNA levels then drop steeply, with junB returning to normal quiescence and the c-myc level remaining slightly elevated during the 3-day culture period. Levels of c-jun mRNA and AP-1 DNA binding activity, however, remain elevated from the outset while C/EBP.alpha. mRNA expression is down-regulated, resulting in a decrease in the steady-state levels of the 42- and 30-kDa C/EBP.alpha. polypeptides and C/EBP.alpha. DNA binding activity. In contrast, C/EBP.beta. mRNA prodn. remains at near-normal hepatic levels for 5 to 8 days of culture, although its DNA binding activity decreases severalfold during this time. Adhesion of hepatocytes to the EHS gel for the same period of time dramatically alters this program: it arrests growth and inhibits AP-1 DNA binding activity and the expression of c-jun, junB, and c-myc mRNAs, but, in addn., it restores C/EBP.alpha. mRNA and protein as well as C/EBP.alpha. and C/EBP.beta. DNA binding activities to the abundant levels present in freshly isolated hepatocytes. These changes are not due merely to growth inhibition, because suppression of hepatocyte proliferation on collagen by epidermal growth factor starvation or addn. of transforming growth factor .beta. does not inhibit AP-1 activity or restore C/EBP.alpha. DNA binding activity to normal hepatic levels. These data suggest that expression of the normal hepatic phenotype requires that hepatocytes exist in a G0 state of growth arrest, facilitated here by adhesion of cells to the EHS gel, in order to express high levels of hepatic transcription factors such as C/EBP.alpha..

L77 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:528183 HCAPLUS
DN 121:128183
TI Purification and characterization of integrin .alpha.9.beta.1
AU Forsberg, E.; Ek, B.; Engstroem, A.; Johansson, S.
CS Biomed. Cent., Univ. Uppsala, Uppsala, S-751 23, Swed.
SO Experimental Cell Research (1994), 213(1), 183-90
CODEN: ECREAL; ISSN: 0014-4827
DT Journal
LA English
AB A new .beta.1-contg. integrin was isolated from rat liver by affinity chromatog. on Sepharose conjugated with the peptide GRGDSPC. The interaction was weakened but not abolished when the arginine and/or aspartic acid in the peptide were replaced with lysine and glutamic acid, resp. In contrast, the cysteine was necessary for binding of the integrin. The .beta.1-assocd. protein, referred to as .alpha.9, had an N-terminal amino acid sequence related to but distinct from previously described integrin .alpha.-subunits. In addn., an internal peptide sequence was obtained which confirmed that the protein is a new member of the family of integrin .alpha.-subunits. An antiserum raised against a synthetic peptide corresponding to amino acids 1-16 of .alpha.9 reacted specifically with this protein and was used to identify .alpha.9 in several tissues. The integrin .alpha.9.beta.1 was not retained on Sepharose conjugates with **Englebreth-Holm-Swarm** tumor (EHS)-laminin, collagen type I, or a 105-kDa cell-binding fragment of fibronectin. However, it did bind specifically to EHS-laminin and collagen type I adsorbed to plastic microtiter wells. The sites of the interactions were localized to fragment E8 of EHS-laminin and to cyanogen bromide fragment 8 of collagen .alpha.1(I) and were not inhibited by sol. RGD-contg. peptides. The results indicate that .alpha.9.beta.1 is a widely distributed laminin/collagen receptor which may have addnl., yet unidentified ligands.

L77 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:319292 HCAPLUS
DN 120:319292
TI Recognition of fibrinogen and basement **membrane** components as mediators of the adherence of Aspergillus fumigatus conidia
AU Bouchara, J. P.; Renier, G.; Coulot, P.; Penn, P.; Tronchin, G.; Chabasse, D.
CS Lab. Parasitologie-Mycologie, Cent. Hospitalier Univ., Angers, 49033, Fr.
SO Colloids and Surfaces, B: Biointerfaces (1994), 2(1-3), 299-304
CODEN: CSBBEQ; ISSN: 0927-7765
DT Journal
LA English
AB In order to elucidate the mol. basis of the adherence of Aspergillus fumigatus to epithelial surfaces, the authors investigated the interactions between this opportunistic fungus and some host adhesive proteins. Among the presumptive ligands, attention was focused on fibrinogen and laminin which are known to mediate the attachment of numerous microorganisms to the host tissues. These interactions were first demonstrated using sol. human fibrinogen and laminin extd. from the **Englebreth-Holm-Swarm** sarcoma tumor. By immunofluorescence and electron microscopy, the binding of these two proteins was detected mainly at the surface of conidia, assocd. with the protrusions of the outer cell wall layer of resting conidia, or uniformly distributed over the cell wall of swollen conidia and of mother cells of germ tubes. Moreover, these interactions seemed to be involved in the adherence of conidia. Conidia strongly adhered to fibrinogen or laminin but not to fibronectin or heparan sulfate proteoglycans immobilized in wells of polystyrene microtiter plates. Adhesion was dose dependent and specific. Binding sites appeared to be located in the D domains of the

fibrinogen mol. and in the fragment P1 of laminin. In addn., flow cytometric anal. of the binding of fibrinogen demonstrated that the expression of binding sites at the surface of conidia correlated with their maturation, and confirmed the specificity of the interaction. Binding was inhibited by unlabeled fibrinogen and by basement **membrane** laminin, suggesting the existence of a common receptor or steric hindrance of the receptor sites by the unresp. ligand. However, precise identification of the adhesiotope failed since no inhibition could be obtained by the different synthetic peptides used nor by the sugars tested.

L77 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:213332 HCAPLUS
DN 120:213332
TI Presence of laminin B chain-like protein in bovine and rat adrenal chromaffin granules
AU Fujino, Yukio; Fujii, Tomoko; Daimon, Tateo
CS Sch. Med., Teikyo Univ., Tokyo, 173, Japan
SO Journal of Biochemistry (Tokyo, Japan) (1994), 115(3), 615-21
CODEN: JOBIAO; ISSN: 0021-924X
DT Journal
LA English
AB The presence of a glycoprotein laminin in bovine adrenal chromaffin granules was examd. by SDS-PAGE followed by immunoblotting. The two chromaffin granule **membrane** fractions were obtained by linear **sucrose** gradient centrifugation followed by freezing and thawing and gel-filtration of the chromaffin granule-rich fraction, resp. The purity of the granules in these fractions was examd. by electron microscopy. These fractions contained laminin B chain-like immunoreactivity as a major immunoreactive component against anti-laminin. Laminin A chain-like immunoreactive protein was undetectable. The sol. fraction of the chromaffin granules contained no immunoreactive peptide. The presence of laminin-like immunoreactivity in the chromaffin granules was confirmed by immunocytochem. study. Laminin B chain-like immunoreactivity was also identified in the rat adrenal chromaffin granule fraction. Laminin A chain was hardly detected, as in the case of bovine adrenals. The structure of laminin in chromaffin granules in bovine and rat adrenals may be different from that of mouse **Englebrethe-Holm-Swarm** sarcoma laminin. The functional significance of laminin B chain-like protein in the granules is unknown at present.

L77 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:51324 HCAPLUS
DN 120:51324
TI A novel sequence in the type IV collagen promoter binds nuclear proteins from Engelbreth-Holm-Swarm tumor
AU Bruggeman, L. A.; Burbelo, P. D.; Yamada, Y.; Klotman, P. E.
CS Lab. Dev. Biol., Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SO Oncogene (1992), 7(8), 1497-502
CODEN: ONCNES; ISSN: 0950-9232
DT Journal
LA English
AB The prodn. of **extracellular matrix** proteins is an important element of tumor formation, and alterations in **matrix** protein metab. may be crit. to the process of tumor metastasis. Abundant expression of type IV collagen, the major structural protein of the basement **membrane**, is characteristic of the **Englebreth-Holm-Swarm** (EHS) mouse sarcoma. In the present study, the mechanisms of transcriptional regulation of type IV collagen genes were evaluated by analyzing nuclear factors that bind to the promoter region. Gel mobility-shift assays indicated that specific proteins from EHS tumor bound the promoter and generated several unique shift patterns. The specific sequences to which these protein bound were

detd. using DNAse I protection assays. DNA-binding proteins protected two regions from DNAse I digestion. The first region was similar to a GC box, the binding site for the transcription factor Sp1. The other footprint was a 30-bp region that contained the novel sequence motif, 'CCCTCCC' present in several other **extracellular matrix** promoters. Nuclear exts. isolated from tissues that variably express type IV collagen bound to this protected sequence with distinctly different shift patterns. Furthermore, in highly expressing tissues, unlabeled oligonucleotides contg. the 'CCCTCCC' motif effectively inhibited nuclear protein binding with the entire promoter. Thus, it is likely that a novel protein or protein complex binds to these sequences. Furthermore, these sequences appear to be unique to the genes that encode basement **membrane** proteins, suggesting a specific role in their regulation.

L77 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:641529 HCAPLUS
DN 119:241529
TI Growth of separated and recombined neonatal rat uterine luminal epithelium and stroma on **extracellular matrix**: effects of in vivo tamoxifen exposure
AU Branham, William S.; Lyn-Cook, Beverly D.; Andrews, Annette; Sheehan, Daniel M.
CS Div. Reprod. Dev. Toxicol., Natl. Cent. Toxicol. Res., Jefferson, AR, 72079, USA
SO In Vitro Cellular & Developmental Biology: Animal (1993), 29A(5), 408-14 CODEN: IVCAED; ISSN: 1071-2690
DT Journal
LA English
AB The authors have developed a system for serum-free culture of sepd. uterine epithelium and stroma from 11-day-old rats recombined on **extracellular matrix** extd. from **Englebreth-Holm-Swarm** tumors. Epithelium grew and, after 2 days in culture, developed into luminal epithelial spheres (LES) surrounding a fluid-filled lumen. Individual LES cells maintained epithelial cell characteristics, such as basally located nuclei, apical microvilli (oriented toward the lumen), lateral **membranes** with interdigitations and desmosomes, secretory Golgi complexes, and abundant mitochondria and rough endoplasmic reticulum. Secretory vesicles were ubiquitous throughout the luminal fluid. Addn. of 17.beta.-estradiol to the growth medium increased the no. and longevity of the LES. Prior exposure of uteri to tamoxifen via s.c. injection in vivo on postnatal days 1 to 5 reduced or completely inhibited formation of LES in vitro. These effects occurred regardless of whether the stromal or epithelial component of the recombinant tissue was exposed to tamoxifen. These data suggest a directive property of neonatal stroma in culture resulting in the formation of highly secretory spherical epithelial structures completely enclosing a lumen. LES formation is responsive to both estrogen (pos. response) and antiestrogen (neg. response).

L77 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:556978 HCAPLUS
DN 119:156978
TI Role of laminin in endothelial cell recognition and differentiation
AU Schnaper, H. William; Kleinman, Hynda K.; Grant, Derrick S.
CS Lab. Dev. Biol., Natl. Inst. Dent. Res., Bethesda, MD, USA
SO Kidney International (1993), 43(1), 20-5 CODEN: KDYIA5; ISSN: 0085-2538
DT Journal
LA English
AB The vascular endothelium normally is maintained in a quiescent state, but under certain conditions it is induced to undergo marked changes in behavior and form new vascular structures. A complex interaction among various growth and differentiation factors and the extracellular milieu

regulates this behavior, and this interaction is discussed. One series of signals affecting endothelial behavior is provided by laminin, a major structural protein of basement **membrane**. These signals have been studied using Matrigel, a reconstituted basement **membrane** prepn. from the murine **Englebreth-Holm-Swarm** sarcoma, in an in vitro assay of endothelial cell differentiation. Three biol. active sequences from the laminin mol. have been evaluated. Synthetic peptides that include the sequences -RGD-, -YIGSR-, and -SIKVAV- mediate, resp., cell binding to Matrigel, alterations in cell morphol., and induction of migration and collagenase activity. Preliminary data indicate that observations made with this system may be relevant to endothelial function in vivo. Endothelial cell differentiation on Matrigel may thus be a useful in vitro model for the study of certain steps in angiogenesis.

L77 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1991:532582 HCAPLUS
DN 115:132582
TI Endothelial heparan sulfate proteoglycan. I. Inhibitory effects on smooth muscle cell proliferation
AU Benitz, William E.; Kelley, Richard T.; Anderson, Clay M.; Lorant, Diane E.; Bernfield, Merton
CS Sch. Med., Stanford Univ., Stanford, CA, 94305, USA
SO American Journal of Respiratory Cell and Molecular Biology (1990), 2(1), 13-24
CODEN: AJRBEL; ISSN: 1044-1549
DT Journal
LA English
AB To investigate the hypothesis that factors produced by endothelial cells may regulate smooth muscle cell growth, the effects of culture medium conditioned by fetal bovine pulmonary arterial endothelium were studied on proliferation of smooth muscle cells in culture. This conditioned medium contains an inhibitor of smooth muscle proliferation that is degraded by nitrous acid, heparinase, and heparitinase, but resists degrdn. by protease, boiling, and chondroitin ABC lyase, indicating that the inhibitor is structurally similar to heparin. Inhibitor release occurs in both growing and confluent endothelial cell cultures and in the presence and absence of serum. A growth-inhibiting proteoglycan purified to homogeneity from endothelial cell-conditioned medium has physicochem. characteristics similar to those of the prototypic basement **membrane** heparan sulfate proteoglycan of the **Englebreth-Holm-Swarm** tumor: an overall size of .apprx.106 daltons (D), heparan sulfate chains of 60,000 D, and a buoyant d. of 1.33 g/mL. Antibody raised against the tumor basement proteoglycan recognizes this endothelial heparan sulfate proteoglycan, and Western blotting after SDS-PAGE demonstrates that the core proteins of both proteoglycans migrate as a doublet at apparent mol. wts. of 450,000 and 360,000 D. Heparan sulfate glycosaminoglycan prepd. from purified medium proteoglycan is a potent inhibitor of smooth muscle cell growth, exhibiting activity .apprx.1000-fold greater than that of heparin. These results indicate that endothelial cells cultured from fetal bovine pulmonary arteries produce a basement **membrane** heparan sulfate proteoglycan that is a potent inhibitor of smooth muscle proliferation. This proteoglycan may mediate endothelial regulation of smooth muscle growth during development or pathol. pulmonary arterial remodeling.

L77 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1991:59612 HCAPLUS
DN 114:59612
TI Adhesion, shape, proliferation, and gene expression of mouse Leydig cells are influenced by **extracellular matrix** in vitro
AU Vernon, Robert B.; Lane, Timothy F.; Angello, John C.; Sage, Helene
CS Sch. Med., Univ. Washington, Seattle, WA, 98195, USA

SO Biology of Reproduction (1991), 44(1), 157-70
CODEN: BIREBV; ISSN: 0006-3363
DT Journal
LA English
AB The influence of the **extracellular matrix** (ECM) on adult mouse Leydig cells was examd. by culturing the cells on different ECM substrates. Leydig cells adhere weakly to hydrated gels of type I collagen (including those supplemented with collagen types IV, V, or VIII), or to air-dried films of collagen types I, V, or VIII. In contrast, the cells attach firmly to substrates of purified type IV collagen, fibronectin, or laminin. Leydig cells also attach rapidly and adhere strongly to gelled basement **membrane matrix** derived from the murine **Englebreth-Holm-Swarm** sarcoma (Matrigel). Leydig cells assume spherical shapes and form aggregates on thick (1.5-mm) layers of Matrigel; however, on thin (0.1-mm) layers, networks of cell clusters linked by cords of elongated cells are formed within 48 h. Similar networks are formed on thick layers of Matrigel that are supplemented with type I collagen. On substrates with high ratios of collagen I to Matrigel or on untreated tissue culture plastic, Leydig cells flatten and do not aggregate. On substrates that induce rounded shapes, proliferation is inhibited and the cells maintain the steroidogenic enzyme 3.beta.-hydroxy steroid dehydrogenase for as long as 2 wk. Under conditions where Leydig cells are flattened, they divide and cease expressing the enzyme. Proliferating Leydig cells also exhibit elevated levels of mRNA for SPARC (secreted protein, acidic and rich in cysteine), a Ca2+-binding glycoprotein assocd. with changes in cell shape that accompany morphogenesis and tissue remodeling. Apparently, the shape, assocn., proliferation, and expression of gene products by Leydig cells can be significantly affected in vitro by altering the compn. of the **extracellular** substratum.

L77 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1990:135000 HCAPLUS
DN 112:135000
TI Purification and properties of aldose reductase and aldehyde reductase from EHS tumor cells
AU Tanimoto, Tsuyoshi; Sato, Sanai; Kador, Peter F.
CS Natl. Eye Inst., Natl. Inst. Health, Bethesda, MD, 20892, USA
SO Biochemical Pharmacology (1990), 39(3), 445-53
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
AB **Englebreth-Holm-Swarm** (EHS) tumor cells were utilized as a model for investigating the prodn. of basement **membrane** components. These cells contain 2 immunol. distinct NADPH-dependent reductases, aldose reductase (EC 1.1.1.21) and aldehyde reductase (EC 1.1.1.2), which were purified to apparent homogeneity by a combination of procedures which included ammonium sulfate fractionation, Sephadex G-75 gel filtration, Matrex Gel Orange A affinity chromatog., and chromatofocusing on Pharmacia Mono P. The mol. wts. of aldose and aldehyde reductases were estd. to be 38K and 40K, resp., by SDS-PAGE. Substrate specificity studies showed that both enzymes were capable of reducing a variety of aldehydes to their resp. alcs.; however, only aldehyde reductase oxidized L-gulonic acid. Surprisingly, both enzymes showed similar reactivities with D-glucose and D-galactose, suggesting that both aldose and aldehyde reductases may contribute to sorbitol prodn. in the EHS tumor cell. The activities of both enzymes were increased by the presence of sulfate ion, but Cl- decreased the activity of aldose reductase. Both aldose and aldehyde reductases were inhibited by a series of structurally diverse aldose reductase inhibitors.

L77 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1990:5380 HCAPLUS

DN 112:5380
TI Effects of two **extracellular matrices** on morphologic and biochemical properties of human type II cells in vitro
AU Edelson, J. D.; Shannon, J. M.; Mason, R. J.
CS Dep. Med., Natl. Jew. Cent. Immunol. Resp. Med., Denver, CO, 80206, USA
SO American Review of Respiratory Disease (1989), 140(5), 1398-404
CODEN: ARDSBL; ISSN: 0003-0805
DT Journal
LA English
AB Several aspects of differentiated adult human type II cells cultured on either bovine corneal endothelial cell **extracellular matrix** (BCECM) or **matrix** derived from the **Englebreth-Holm-Swarm** tumor (EHS) were examd. Compared to cells cultured on BCECM, adult human type II cells grown on EHS assumed a more cuboidal shape, had a more defined apical-basal polarity, and appeared to contain a greater no. of lamellar bodies and neutral lipid inclusions. These cells also incorporated a greater percentage of [14C]acetate into satd. phosphatidylcholine (SPC) than did their counterparts grown on BCECM. In contrast, the relative incorporation of [14C]acetate into phosphatidylglycerol (PG) was lower in cells grown on EHS than cells cultured on BCECM. The histochem. stain for alk. phosphatase was useful in identification of human type II cells. Alk. phosphatase expression was elevated in cells cultured on EHS compared to those cultured on BCECM. Apparently, maintenance of a differentiated morphol., lipid synthesis, and expression of alk. phosphatase activity by primary cultures of adult human type II cells are also influenced by cell-**matrix** interactions. All markers of differentiated function of type II cells except synthesis of PG are better maintained on EHS than on BCECM. Under the conditions of these expts., synthesis of SPC and PG appears to be independently regulated.

L77 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1989:511244 HCAPLUS
DN 111:111244
TI The sequence of the mouse 14 kDa .beta.-galactoside-binding lectin and evidence for its synthesis on free cytoplasmic ribosomes
AU Wilson, T. J. Greer; Firth, Malcolm N.; Powell, Janet T.; Harrison, F. Lynne
CS Inst. Anim. Physiol. Genet. Res., AFRC, Babraham/Cambridge, CB2 4AT, UK
SO Biochemical Journal (1989), 261(3), 847-52
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
AB The partial amino acid sequence of the mouse 14-kDa .beta.-galactoside-binding lectin was deduced from cDNA clones corresponding to 86% of the coding sequence and extending to the polyadenylation signal. The deduced amino acid sequence for the murine lectin shows 94% identity with the rat, 89% with human, 86% with bovine, and 46% with the chicken 14-kDa lectins. A cDNA probe was used to analyze genomic DNA and identify a single mRNA of .apprx.570 bp in 3T3 fibroblasts, murine erythroleukemia cells, and the murine basement-**membrane**-secreting **Englebreth-Holm-Swarm** tumor. Anal. of free and bound polyribosomes has shown that the lectin message is translated on free cytoplasmic ribosomes.

L77 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1989:490763 HCAPLUS
DN 111:90763
TI Laminin induces formation of neurite-like processes and potentiates secretion by GH3 rat pituitary cells
AU Brunet-De Carvalho; Picart, Renee; Van de Moortele, Solange; Tougard, Claude; Tixier-Vidal, Andree
CS Groupe Neuroendocrinol. Cell. Mol., Coll. France, Paris, F-75231/5, Fr.

SO Differentiation (Berlin, Germany) (1989), 40(2), 106-18
CODEN: DFFNAW; ISSN: 0301-4681
DT Journal
LA English
AB Laminin extd. from **Englebreth-Holm-Swarm** (EHS) tumors was a potent attachment and spreading factor for GH3/B6 cells seeded in serum-free medium. Moreover, it induced the formation of neurite-like processes, which were increased in no. and length by chronic treatment with a specific secretagogue, thyroliberin (TRH). These changes in cell shape were correlated with a potentiation of prolactin secretion, both basal and TRH-stimulated. Furthermore by using immunocytochem. and electron microscopy, it was revealed - at the dilated tip of processes - an accumulation not only of prolactin, but also of synaptophysin, a vesicle **membrane** marker, and of several organelles, such as secretory granules, smooth vesicles, dense bodies, and mitochondria. The cytoplasmic processes contained long parallel bundles of microtubules and showed a strong immunoreactivity for .beta.2-tubulin. In addn., immunocytochem. evidence was found for the presence of 200-kDa neurofilament protein in GH3/B6 cell processes as well as in neurites of cultured hypothalamic neurons. Thus, in GH3/B6 cells, laminin induced the differentiation of neurite-like processes, which were the site of polarized organelle transport and exhibited some neuronal markers.

L77 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1989:170914 HCAPLUS
DN 110:170914
TI Matrix-derived soluble components influence type II pneumocytes in primary culture
AU Rannels, Stephen R.; Grove, Rhea N.; Rannels, D. Eugene
CS Coll. Med., Pennsylvania State Univ., Hershey, PA, 17033, USA
SO American Journal of Physiology (1989), 256(3, Pt. 1), C621-C629
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English
AB Type II pulmonary epithelial cells cultured on a plastic surface fail to retain differentiated form and function. During the 1st 3 days in primary culture, the cells flatten and lose characteristic lamellar inclusions; they increase in size and exhibit accelerated rates of protein synthesis and thymidine incorporation. These transitions are inhibited markedly if the cells are plated on Matrigel (MG), a laminin-rich surface derived from the **Englebreth-Holm-Swarm** sarcoma. Sol. components released from MG (MGS) mimic some of the effects of the solid gel. As on a plastic surface, the cells flatten when exposed to MGS during culture. In contrast, MGS inhibits thymidine incorporation and protein synthesis; it is most effective when added early in the culture interval. Direct contact of the cells with the MG surface itself is always more effective than maximal MGS activity. The effects of MGS are not reproduced by purified laminin or by transforming growth factor-.beta., both of which are present in MG. Apparently, the effects of the solid MG surface on cell morphol. are caused in part by direct cell-matrix contact, but addnl. effects, such as decreased DNA synthesis, can be mediated by activity of solubilized gel components. They further provide a model wherein changes in type II cell morphol. and function, which typically occur in parallel during primary culture, can be sepd. exptl.

L77 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1989:5209 HCAPLUS
DN 110:5209
TI Alkaline phosphatase: a marker of alveolar type II cell differentiation
AU Edelson, Jeffrey D.; Shannon, John M.; Mason, Robert J.
CS Sch. Med., Univ. Colorado, Denver, CO, USA
SO American Review of Respiratory Disease (1988), 138(5), 1268-75

CODEN: ARDSBL; ISSN: 0003-0805
DT Journal
LA English
AB To identify type II cells by a method independent of staining phospholipid inclusions, a histochem. technique for alk. phosphatase (I) activity was evaluated in normal rat lung, in freshly isolated type II cells, and in primary culture of type II cells. In the adult rat alveolus, I staining selectively identified type II cells, although nonciliated bronchiolar (Clara) cells and loose perivascular connective tissue also stained for I activity. In cell suspensions of type II cells and other dissocd. lung cells, I staining correlated closely with the modified Papanicolaou technique and was particularly useful in distinguishing type II cells from alveolar macrophages. To det. if I was related to the differentiated phenotype of type II cells, conditions known to affect other type II cell functions were studied. When type II cells were cultured on plastic substrata, the intensity of I staining decreased with increasing time in culture. To quantitate the apparent decrease in I activity, a biochem. assay was used to study the expression of I by type II cells. The specific activity of I in type II cells declined with increasing time in tissue culture on plastic substrata. I activity was maintained, however, by culturing cells on **Englebreth-Holm-Swarm** (EHS) tumor matrix. Cells that had reduced levels of I activity following 48 h of culture on plastic substrata could be rescued by removing them from the plastic substratum and reculturing them for 48 h on EHS matrix. I activity was also increased by culturing type II cells in the presence of cAMP or Na butyrate. By examg. prepns. of fetal rat lung low I levels were found early in gestation and an increase at the end of gestation. The development peak of I activity occurred 2 days before term in the rat. I expression by type II cells appears to be regulated in concert with the synthesis of the phospholipid and apoprotein components of pulmonary surfactant in both adult type II cells in primary culture and in the fetal lung. Although its physiol. function remains unknown, it is postulated that I expression represents a marker of differentiated function of type II cells.

L77 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1988:145782 HCAPLUS
DN 108:145782
TI Glomerular basement **membrane** proteoglycans are derived from a large precursor
AU Klein, David J.; Brown, David M.; Oegema, Theodore R.; Brenchley, Paul E.; Anderson, John C.; Dickinson, Mark A. J.; Horigan, Elizabeth A.; Hassell, John R.
CS Dep. Pediatr., Univ. Minnesota, Minneapolis, MN, 55455, USA
SO Journal of Cell Biology (1988), 106(3), 963-70
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
AB The basement **membrane** heparan sulfate proteoglycan produced by the **Englebreth-Holm-Swarm** (EHS) tumor and by glomeruli were compared by immunol. methods. Antibodies to the EHS proteoglycan immunopptd. a single precursor protein (mol. wt. = 400,000] from [35S]methionine-pulsed glomeruli, the same size produced by EHS cells. These antibodies detected both heparan sulfate proteoglycans and glycoproteins in exts. of unlabeled glomeruli and glomerular basement **membrane**. The proteoglycans contained core proteins of varying size (mol. wt. = 150,000-400,000) with a 250,000-dalton species being predominant. The glycoproteins were fragments of the core protein which lacked heparan sulfate side-chains. Antibodies to glomerular basement **membrane** proteoglycan immunopptd. the precursor protein (mol. wt. = 400,000) synthesized by EHS cells and also reacted with most of the proteolytic fragments of the EHS proteoglycan. The antibody did not, however, react with the P44 fragment, a peptide situated at one end of the

EHS proteoglycan core protein. The data suggest that the glomerular basement **membrane** proteoglycan is synthesized from a large precursor protein which undergoes specific proteolytic processing.

L77 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1988:72861 HCAPLUS
DN 108:72861
TI **Extracellular matrix** fibers containing fibronectin and basement **membrane** heparan sulfate proteoglycan coalign with focal contacts and microfilament bundles in stationary fibroblasts
AU Singer, Irwin I.; Scott, Solomon; Kawka, Douglas W.; Hassell, John R.
CS Merck, Sharp, and Dohme Res. Lab., Merck Co., Inc., Rahway, NJ, 07065, USA
SO Experimental Cell Research (1987), 173(2), 558-71
CODEN: ECREAL; ISSN: 0014-4827
DT Journal
LA English
AB Double-label immunofluorescence microscopy and immunoelectron microscopy were performed on stationary cultures of Nil 8 fibroblasts to det. if fibronectin and basement **membrane** heparan sulfate proteoglycans play coordinated roles in cell-to-substrate adhesion. Relationships between subcellular **matrix** fibers contg. fibronectin plus proteoglycan, and focal contacts assocs. with microfilament bundles, were studied simultaneously by using interference reflection microscopy, differential interference contrast microscopy, and immunofluorescence microscopy. Cells maintained in 0.3% fetal bovine serum were doubly stained with monospecific anti-fibronectin IgG and antibodies against a basement **membrane** proteoglycan purified from the EHS (**Englebreth-Holm-Swarm**) tumor. Coincident patterns of fibronectin- and proteoglycan-contg. fibers were codistributed with focal contacts and microfilament bundles in both early (6-h) and late (24-h) cultures. The early cells showed doubly-stained fibers colinear with substrate adhesion sites in 43% of the sample, whereas 100% of the later cells exhibited these coaligned **matrix**-cytoskeletal attachment complexes. Immunoelectron microscopy showed that both of these antigens were situated in the same type of **extracellular matrix** fiber that appeared to be loosely assocd. with the cell surface **membrane**. The appearance of proteoglycan in subcellular **matrix** fibers of these fibroblasts might stabilize fibronectin-contg. cell-to-substrate contacts.

L77 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1988:72777 HCAPLUS
DN 108:72777
TI Regulation of rat mammary gene expression by **extracellular matrix** components
AU Blum, Joanne L.; Zeigler, Mary E.; Wicha, Max S.
CS Simpson Mem. Res. Inst., Univ. Michigan, Ann Arbor, MI, 48109, USA
SO Experimental Cell Research (1987), 173(2), 322-40
CODEN: ECREAL; ISSN: 0014-4827
DT Journal
LA English
AB In primary rat mammary cultures the effects of a basement **membrane** gel derived from the **Englebreth-Holm-Swarm** tumor as well as its major component, laminin, on the expression of a group of milk protein genes were examd. The basement **membrane** gel induces .alpha.-casein and .alpha.-lactalbumin (.alpha.-LA) accumulation .ltoreq.160- and 70-fold, resp., of that on tissue culture plastic. Laminin, a major component of the basement **membrane**, also caused significant induction of these same proteins. Pulse-chase expts. demonstrated that a laminin substratum selectively affects milk protein turnover and secretion. To demonstrate whether **extracellular matrix** (ECM) effects occurred at the level of steady-state accumulation of mRNA, dot blot and Northern blot analyses

were performed by using cloned cDNA probes for .alpha.-, .beta.-, and .gamma.-caseins and .alpha.-LA . ECM components induced .alpha.- and .beta.-caseins .ltoreq.10-fold, and .alpha.-LA .ltoreq.3-fold, with no significant effect on .gamma.-casein. Thus, milk protein genes are not coordinately regulated by ECM components. Furthermore, since the amt. of induction of milk proteins exceeds the amt. of induction of mRNAs for these proteins, in the present system a major effect of ECM components is at the translational and(or) posttranslational level. Based on these findings, a model in which basement **membrane** components regulate mammary gene expression at multiple levels is proposed.

L77 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1987:613779 HCAPLUS
DN 107:213779
TI Self-assembly of a high molecular weight basement **membrane** heparan sulfate proteoglycan into dimers and oligomers
AU Yurchenco, Peter D.; Cheng, Yi Shan; Ruben, George C.
CS Robert Wood Johnson Med. Sch., Univ. Med. Dent., Piscataway, NJ, 08854, USA
SO Journal of Biological Chemistry (1987), 262(36), 17668-76
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB A high-mol.-wt. basement **membrane** heparan sulfate proteoglycan, isolated from murine **Englebreth-Holm-Swarm** tumor, is seen in Pt replicas as an elongated flexible core (mol. wt., Mr = 450,000) consisting of a series of tandem globular domains from which extend, at one end, 2-3 heparan sulfate chains (av. Mr = 80,000 each). This macromol. will self-assemble into dimers and lesser amts. of oligomers when incubated in neutral isotonic **buffer**. These mol. species can be sepd. by zonal velocity sedimentation and assembly is seen to be time and concn. dependent. In rotary-shadowed Pt replicas, the binding region is found at or near the end of the core at the pole opposite the origin of the heparan sulfate chains. Dimers are double-length structures and oligomers are seen as stellite clusters: in both, the heparan sulfate chains appear peripherally oriented. Whereas isolated cores self-assemble, isolated heparan sulfate chains do not bind intact proteoglycans. Furthermore, proteolytic removal of a nonheparan sulfate-contg. core moiety destroys the ability of the proteoglycan monomer to form larger species or bind intact proteoglycan, further supporting the binding topog. detd. morphol. These neg. charged macromol. complexes may be important contributors to basement **membrane** structure and function.

L77 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1987:80550 HCAPLUS
DN 106:80550
TI Domain structure of the basement **membrane** heparan sulfate proteoglycan
AU Ledbetter, Steven R.; Fisher, Larry W.; Hassell, John R.
CS Upjohn Pharm. Co., Kalamazoo, MI, 49007, USA
SO Biochemistry (1987), 26(4), 988-95
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Proteolytic digestions and immunol. reactivity were used to map regional domains of the 400-kilodalton (kDa) core protein of the heparan sulfate-contg. basement **membrane** proteoglycan from the **Englebreth-Holm-Swarm** (EHS) tumor. Digestion with V8 protease caused the rapid release of numerous large peptides of 80-200 kDa; a 44-kDa peptide (P44) was stable to further digestion, but the larger peptides were eventually degraded to a 46-kDa peptide (P46). Both the P44 and P46 fragments migrate more slowly in the presence of a

reducing agent than in its absence, indicating intrachain SS bonding, and neither has heparan sulfate side chains. Antisera to the P46 fragment, however, did not react with the P44 fragment, and the amino acid compn. of P46 and P44 fragments were different, suggesting that these 2 fragments are unrelated. Trypsin digestion of the proteoglycan immediately released a 200-kDa peptide (P200) that also lacked heparan sulfate side chains. Digestion of the P200 fragment with V8 protease produced the P44 and P46 fragments in the same temporal sequence seen with V8 protease digestion of the proteoglycan. Antisera to the P200 fragment reacted strongly with both the P44 and P46 fragments. The P44 and P46 domains are thus contained within the P200 domain. The rapid release of the P44 domain indicates that it is located at one end of the core protein. The large size of these proteolytic fragments suggests the core protein contains considerable conformational structure, and the absence of heparan sulfate on the P200 domain indicates that the side chains are asym. located on the core.

L77 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1986:607247 HCAPLUS
DN 105:207247
TI Antibody specificity of human glomerular basement **membrane** type IV collagen NC1 subunits. Species variation in subunit composition
AU Kleppel, Mary M.; Michael, Alfred F.; Fish, Alfred J.
CS Dep. Lab. Med. Pathol. Pediatrics, Univ. Minnesota, Minneapolis, MN, 55455, USA
SO Journal of Biological Chemistry (1986), 261(35), 16547-52
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB NC1 subunits (globular domains formed by the interactions of the C-terminal propeptide trimers of type IV collagen) were purified from gel filtration pools of acid-extd., collagenase-digested human glomerular basement **membranes** (hGBM). This methodol., which enriches 28-kilodalton (kDa) monomers (M28) in the total digest, allowed purifn. of these monomers and 24-kDa (M24) and 26-kDa (M26) monomers free from dimers. Reactivity of these subunits with Goodpasture autoantibodies showed strong reactivity with the purified M28 subunits. Comparison of hGBM NC1 components were made with those obtained from collagenase digests of salt and acid-extd. bovine and sheep GBM and **Englebreth-Holm-Swarm** tumor similarly purified by gel filtration and reverse-phase HPLC. Two-dimensional gel anal. of these NC1 isolates revealed absence of the very cationic M28 monomers. Reactivity with antibodies eluted from diseased kidneys of sheep immunized with hGBM (Steblay nephritis) was compared with Goodpasture autoantibody reactivity by immunoblotting 2-dimensional gels of hGBM NC1. A very cationic M28 monomer (M28+++) found only in hGBM was the probable target in Goodpasture syndrome. The epitope was present on most NC1 components from extd. and unextd. hGBM, and was exposed by urea denaturation which was enhanced by acid treatment. A weakly cationic M28 monomer (M28+) was present in GBM from other species and was the probable target in Steblay nephritis. Differential recognition of the 2 M28 components by these antibodies points to different genetic origins or possibly distinct post-translational modifications for these components. This is supposed by their presence or absence in different species and tissues, as well as biochem. differences from the M24/26 monomers which presumably are derived from .alpha.1(IV) and .alpha.2(IV) collagen chains.

L77 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1986:146073 HCAPLUS
DN 104:146073
TI .beta.-D-Xyloside-mediated alteration in the synthesis of basement **membrane** proteoglycan
AU Ledbetter, Steven R.; Hassell, John R.

CS Lab. Dev. Biol. Anomalies, Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SO Archives of Biochemistry and Biophysics (1986), 246(1), 403-10
CODEN: ABBIA4; ISSN: 0003-9861
DT Journal
LA English
AB The effect of nitrophenyl-.beta.-D-xyloside (xyloside), a synthetic initiator of glycosaminoglycan synthesis, on proteoglycan and glycosaminoglycan synthesis by a basement **membrane**-producing tumor (**Englebreth-Holm-Swarm** tumor) was studied. Although xyloside markedly stimulated the formation of chondroitin sulfate chains, it depressed the formation of a basement **membrane** heparan sulfate proteoglycan and caused only little formation of free heparan sulfate chains. However, when the synthesis of the core protein of the proteoglycan was inhibited by cycloheximide, heparan sulfate chains were produced by xyloside treatment. These heparan sulfate chains had a sulfate content higher than that of heparan sulfate found on the proteoglycan. Apparently, xyloside can substitute for the heparan sulfate initiation site on the core protein of the proteoglycan, and this initiation is enhanced in the absence of core protein. Thus, under normal conditions the formation of heparan sulfate chains may be tightly linked to the prodn. of the core protein.

L77 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2003 ACS
AN 1985:450048 HCAPLUS
DN 103:50048
TI Biosynthesis of heparan sulfate. Formation of a glycosaminoglycan precursor
AU Silbert, Jeremiah E.; Baldwin, Clinton T.
CS Connect. Tissue-Aging Res. Lab., Veterans Adm. Outpatient Clin., Boston, MA, 02108, USA
SO Glycoconjugate Journal (1984), 1(1), 63-71
CODEN: GLJOEW; ISSN: 0282-0080
DT Journal
LA English
AB Microsomal prepns. from **Englebreth-Holm-Swarm** mouse sarcoma were incubated with UDP-N-acetyl[3H]glucosamine and UDP-[14C]glucuronic acid to form proteoglycan contg. [3H,14C]glycosaminoglycan with equimolar amts. of [3H]glucosamine and [14C]glucuronic acid. The labeled glycosaminoglycan was totally resistant to degrdn. by testicular hyaluronidase, but could be degraded readily by a crude Flavobacter heparinum enzyme prepn. which is capable of degrading heparin and heparan sulfate. Chromatog. of the [3H,14C]glycosaminoglycan on DEAE-cellulose provided a pattern with 3 peaks, the 1st appearing before hyaluronic acid, the 2nd and largest appearing at the site of hyaluronic acid, and a 3rd appearing slightly beyond hyaluronic acid but before a std. of chondroitin sulfate. When 3'-phosphoadenosine 5'-phosphosulfate was also included in the reaction mixt., a change appeared in the [3H,14C]glycosaminoglycan such that chromatog. on DEAE-cellulose presented a pattern with a significant amt. of material which cochromatographed in the area where heparan sulfate would be found. There was no material that cochromatographed with the more highly sulfated substance, heparin. Apparently, the microsomal prepn. from the **Englebreth-Holm-Swarm** sarcoma is capable of producing a heparan sulfate-like mol. and is controlled in its sulfation of precursors so that heparin is not formed.

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http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d l108 all abeq tech abex tot

L108 ANSWER 1 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2002-445985 [48] WPIX
DNC C2002-127165
TI **Coated membrane** for assessing invasiveness of cells, useful e.g. for studying toxicity, comprises porous **membrane** coated with reconstituted extracellular matrix.
DC A89 B04 D16
IN FLAHERTY, P; ILSLEY, S R; KRAMER, M L; MANNUZZA, F J; ILLSLEY, S R
PA (BECT) BECTON DICKINSON & CO; (FLAH-I) FLAHERTY P; (ILSL-I) ILSLEY S R; (KRAM-I) KRAMER M L; (MANN-I) MANNUZZA F J
CYC 30
PI EP 1195432 A2 20020410 (200248)* EN 8p C12N005-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
AU 2001076107 A 20020328 (200248) C12M003-04 <--
CA 2357846 A1 20020327 (200248) EN C12Q001-02
US 2002119560 A1 20020829 (200259) C12M001-34 <--
JP 2002320472 A 20021105 (200304) 21p C12M003-00 <--
ADT EP 1195432 A2 EP 2001-122845 20010924; AU 2001076107 A AU 2001-76107 20010926; CA 2357846 A1 CA 2001-2357846 20010927; US 2002119560 A1 Provisional US 2000-235712P 20000927, US 2001-942349 20010829; JP 2002320472 A JP 2001-297035 20010927
PRAI US 2001-942349 20010829; US 2000-235712P 20000927
IC ICM **C12M001-34; C12M003-00; C12M003-04;** C12N005-00; C12Q001-02
ICS **C12M003-00**
AB EP 1195432 A UPAB: 20020730
NOVELTY - A **coated membrane** (A) for assessing the invasive capacity of a cell comprising a porous **membrane** having, on its surface, a composition (B) consisting of reconstituted and aggregated extracellular matrix (ECM) from the **Englebreth-Holm-Swarm** mouse tumor, pH 7.8-8.2 buffer and a **polyol** (I), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an assembly for assessing invasive capacity of cells that includes (A); and
(2) method for preparing (A).
USE - The device is used to measure invasion of cells through aggregated ECM, e.g. for studying bioavailability, toxicity, or migration, attachment, growth and invasiveness of cells.

ADVANTAGE - (B) provides a uniform and clear coating, and thus even invasion over its entire surface, and is readily digested by invasive cells, but resists passage of non-invasive cells, allowing easy and accurate differentiation between these cell types. (B) mimics the natural basement **membrane** and provides the proper environment for growth, attachment and penetration of cells. The coating is stable for at least 4 weeks at 4 deg. C (contrast 1 week for similar coatings prepared using pH 7.4 phosphate buffer) and addition of (I) prevents precipitation of salt (responsible for non-uniformities).
Dwg.0/7

FS CPI
FA AB; DCN
MC CPI: A12-L04; A12-W11L; **B04-C03**; B04-F02A; B05-A01B; B07-A02A; **B10-B03B**; **B11-C08C**; B11-C08E; B11-C09; B12-K04; D05-H08; D05-H09; D05-H10
TECH UPTX: 20020730
TECHNOLOGY FOCUS - BIOLOGY - Preferred **Membrane**: (A) may also include a salt and has been dried.
Preparation: A solution of ECM is prepared in a **sucrose** -containing buffer (especially about pH 8), then applied to one or both surfaces of a porous **membrane**, and aggregation of the solution components induced, e.g. by incubation for 1-4 hours at 33-40 degrees C and 40-60% relative humidity. The resulting aggregated coating is then stabilized by drying. The ECM loading is 60-100 microgram cm-2.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Buffer: This comprises Tris hydrochloride, at 0.01-0.05M; a salt (particularly sodium chloride at 0.08-0.15M) and **sucrose**, at 2-8wt.%.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Assembly: This comprises a tissue culture plate with wells, an insert designed to fit the plate and having openings at the base and (A) to provide a bottom wall for the openings. It may also include a lid that fits over and seals the insert and a feeder tray designed to receive the insert.

TECHNOLOGY FOCUS - POLYMERS - Preferred **Membrane**: The porous **membrane** is specifically made of **poly(ethylene terephthalate)**, **PET**, particularly track-etched **PET** of thickness 0.5-30, especially 8, microns and pore diameter 3-12 microns.
ABEX UPTX: 20020730
EXAMPLE - A solution containing 2-8wt.% **sucrose** and 0.08-0.15 M sodium chloride in 0.01-0.05 M Tris hydrochloride buffer (pH 7.8-8.2) was mixed, at 0-10 degrees C, with enough extracellular matrix from **Englebreth-Holm-Swarm** mouse tumor to provide 10-150, preferably 65-105, microgram cm-2 of **membrane** after coating. The solution was applied to porous track-etched **poly(ethylene terephthalate) membrane**, incubated at 33-40 degrees C and 40-60% relative humidity for 1-3 hours (for aggregation), then stabilized by drying at 25-30 degrees C and 40-50% relative humidity. The coated **membrane** was fixed across the open ends of the sleeve part of a Falcon (RTM) insert and tested for cell invasion as described in Technical Bulletin 427 (Becton Dickinson). Permeability was 10-24% for the standard non-invasive cell NIH 3T3 and 92-99% for the standard invasive cell HT-1080.

L108 ANSWER 2 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2001-460208 [50] WPIX
DNN N2001-341259 DNC C2001-139477
TI Cell culture film for cultivating liver cells, comprises a copolymer of polyamino acid and urethane, with specific amino acid units coupled continuously.
DC A96 B04 D16 D22 P34

PA (KEIZ-N) KEIZAI SANGYOSHO SANGYO GIJUTSU SOGO KEN; (MITU) MITSUBISHI CHEM CORP
CYC 1
PI JP 2001136960 A 20010522 (200150)* 7p C12N005-06 <--
ADT JP 2001136960 A JP 1999-328500 19991118
PRAI JP 1999-328500 19991118
IC ICM **C12N005-06**
ICS A61L027-00; A61L031-00; C08G018-60; **C12M003-00**; C12N011-08
AB JP2001136960 A UPAB: 20010905
NOVELTY - A cell culture film is formed of a copolymer of polyamino acid and urethane, where the polyvinyl acid has an average of 4 or more amino acid units coupled continuously.
USE - The film is used for cultivating liver cells (claimed).
ADVANTAGE - The film has an excellent cell adhesion property and anti-thrombotic property.
Dwg.0/0
FS CPI GMPI
FA AB; DCN
MC CPI: A05-F03; A05-G01E; A12-V01; B04-C01A; **B04-C03**; B04-F02; B11-C; D05-H02; D09-C01C
TECH UPTX: 20010905
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Source: The polyamino acid urethane resin is obtained by reacting a copolymer of polyamino acid, urethane, alpha-amino acid-N-carboxylic acid anhydride and at least water, hydrazine and organic amine.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: The cell culturing is performed by placing the cell culture film on a polytetrafluoroethylene base material.
ABEX UPTX: 20010905
EXAMPLE - (In g) Polytetra methylene ether **glycol** (980), tolylene diisocyanate (mixture of 2,4-tolylene diisocyanate (80 weight percent) and 2,6-tolylene diisocyanate) (174) were reacted at 70 degreesC for 5 hours to obtain urethane prepolymer having an isocyanate group at its terminal. The obtained urethane prepolymer (58.2) and (gamma)-methyl-L-glutamate (58.2) were dissolved in dimethyl formamide (394.3) to obtain polyamino acid urethane resin solution with a viscosity of 18500 cp at 25 degreesC. Dimethyl formamide (50 parts) was added with polyamino acid urethane resin solution (100 parts), in a glass plate and subsequently dried for 30 minutes at 80 degreesC to form a film. The film was removed completely and processed at 50 degreesC for 2 hours and immersed in water for 50 hours at 20-25 degreesC to obtain a film thickness of 40-45 microm. Liver cells of a rat were cultivated in the obtained film and the results showed that the film had an excellent cultivation property.

L108 ANSWER 3 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 1995-177525 [23] WPIX
DNC C1995-082253
TI Self-contained trans-**membrane** co-culture system - has plugged tube with microporous **membrane** making interference fit in tubular housing with sealing lids..
DC A96 B04 D16
IN GRAY, H E; MUSSI, E F
PA (BECT) BECTON DICKINSON CO
CYC 1
PI US 5409829 A 19950425 (199523)* 9p C12N005-00 <--
ADT US 5409829 A US 1993-124415 19930921
PRAI US 1993-124415 19930921
IC ICM **C12N005-00**
ICS **C12M003-06**
AB US 5409829 A UPAB: 19950619
Self-contained trans-**membrane** co-culture system comprises a tube

(10) with an outwardly flanged end open and the other closed by a microporous **membrane** (18), and a plug (32) making an interference fit in the tube. The **membrane** end of the tube is inserted into a tubular housing (34) and makes an interference fit with an intermediate diameter of the housing. The housing ends are reclosably sealed with gas-permeable lids (58,60) preventing entry of microorganisms. The tube is pref. of **PET**, PE, polycarbonate or polystyrene, and the housing and plug are of polypropylene, PE, **PET**, **glycol**-modified **PET** or PVC. The co-culture method is claimed.

USE - E.g. for studying interactions between cells in relation to inflammatory responses.

ADVANTAGE - Provides a sterile ready-to-use system.

Dwg.4/5

FS CPI
FA AB; GI; DCN
MC CPI: A12-V03C2; A12-W11L; **B04-C03**; B04-F01; B11-A; B12-K04A; B14-C03; D05-H02

L108 ANSWER 4 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 1992-060490 [08] WPIX
DNC C1992-027303
TI Base material for culturing cells - for use in mfr. of hybrid artificial organs or blood vessels.
DC A96 B04 D16
PA (TORA) TORAY IND INC
CYC 1
PI JP 04004869 A 19920109 (199208)*
JP 3139004 B2 20010226 (200120) 5p C12N005-06 <--
ADT JP 3139004 B2 JP 1990-105878 19900420
FDT JP 3139004 B2 Previous Publ. JP 04004869
PRAI JP 1990-105878 19900420
IC **C12M003-00; C12N005-06**
ICM **C12N005-06**
ICS **C12M003-00**
AB JP 04004869 A UPAB: 19931006
The base material for culturing cells composed of the pt. (A) where the contact angle of advance to water is 20-50 deg. and the part (B) where the contact angle of advance to water is 50-100 deg. is new.

Pref. pt. (A) is composed of hydrogel. The pt. (B) is composed of polyolefin or polyester. Pref. pt. (A) composed of hydrogel of cellulose, polyacrylamide, polyethylene **glycol**, hydroxyethylmethacrylate or PVC contg. 30-98 wt.% polyvinyl pyrrolidone is obtd. by modifying a film of the base material having the higher contact angle of advance to water, which is composed of e.g. PVC, polyolefin or polyester, by grafting or coupling it with a hydrophilic polymer, pref. polyethylene oxide.

USE/ADVANTAGE - The base material for culturing cells can culture cells on the condition nearly in vivo. The cells obtd. from it are used for mfg. hybrid artificial organs, e.g. artificial skin, an artificial liver or an artificial blood vessel.

0/2

FS CPI
FA AB; DCN
MC CPI: A12-W11L; B04-B04A3; B04-C02A1; **B04-C03**; D05-H01; **D05-H08**; D09-C01

L108 ANSWER 5 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 1988-273891 [39] WPIX
DNN N1988-208022 DNC C1988-121838
TI Base used to culture cells - obtd. by carrying at least 2 of **sugar**, protein, lipid and glyco protein, on surface of high mol. base.
DC A97 B04 D16 D22 P73
PA (SUME) SUMITOMO ELECTRIC IND CO

CYC 1
PI JP 63198981 A 19880817 (198839)* 8p
ADT JP 63198981 A JP 1987-32233 19870213
PRAI JP 1987-32233 19870213
IC B32B005-18; B32B009-00; C08J007-00; **C12M003-00**; **C12N005-02**; C12N011-02
AB JP 63198981 A UPAB: 19930923
Base is prepd. by carrying at least two kinds of cPds. selected from **sugar**, protein, lipid and their complex cpds. (glycoprotein) on the surface of high molecular base of prescribed arrangement. Pref. porous high molecular base is in hollow fibre form is used. Pref. the surface of high molecular base is pretreated chemically or physically. It is pref. to stratify glycoprotein, etc. with prescribed pattern.
The chemical treatment is used to introduce various functional gps. e.g. carbonyl gp., carboxyl gp., sulphonic gps., nitro gp., amino gp., thiol gp., hydroxyl gp., etc. in the base.
USE/ADVANTAGE - At least two kinds of glycoprotein are carried on the base. It can be used to control adhesive of cells. Glycoprotein has good affinity and adhesive to cells. By using it, cell culture can produce useful cpds. like hormones. It may be used as artificial organs.
0/1
FS CPI GMPI
FA AB
MC CPI: A11-C04D; A11-C04E; A12-S05A; A12-V02; A12-W11L; B04-B01B; B04-B02D; B04-B04A; **B04-C03**; B04-D01; B11-A; D05-C; D05-H02; **D05-H10**; D09-C01C

L108 ANSWER 6 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 1988-273889 [39] WPIX
DNN N1988-208020 DNC C1988-121836
TI Base used to culture cell - obtd. by treating surface of high mol. base with plasma, sputtering, gamma-rays, ozone or chemicals and carrying **sugar**, protein, etc..
DC A97 B04 D16 D22 P73
PA (SUME) SUMITOMO ELECTRIC IND CO
CYC 1
PI JP 63198979 A 19880817 (198839)* 7p
ADT JP 63198979 A JP 1987-32231 19870213
PRAI JP 1987-32231 19870213
IC B32B005-18; B32B009-00; C08J007-00; **C12M003-00**; **C12N005-02**; C12N011-02
AB JP 63198979 A UPAB: 19930923
Base is prepd. by (a) treating the surface of high mol. base wholly with plasma, sputtering, gamma-ray, ozone or chemicals, (b) treating it partly with UV-ray, electronic ray or ion and (c) carrying **sugar**, protein, lipid and their complex such as glycoprotein on it. It is pref. to use porous high mol. base and hollow fibre-form high mol. base. It is pref. to treat the surface of high mol. base partly with UV-ray, etc. in fretwork, striped pattern or polka dots. As collagen is pref. gelatin, fibronectin, laminin, chondronectin, fibrin, etc.
USE/ADVANTAGE - By surface treating with plasma, etc., hydrophilic functional gps. are introduced in the surface of high molecular base and by treating it further with UV-ray, etc. partly in fine pattern, glycoprotein, etc. can be tightly fixed to it. Being fixed and keeping high dimensional structure, glycoprotein, etc. give good adhesive to cells. Thus by using it, cell culture can continue to keep high cell density. It can be used to culture cells producing useful substances, e.g. hormone.
0/1
FS CPI GMPI
FA AB
MC CPI: A11-C04D; A11-C04E; A12-S05A; A12-V02; A12-W11L; B04-B01B; B04-B02D; B04-B04A6; **B04-C03**; B04-D01; B11-A; D05-C; D05-H02;

D05-H10; D09-C01C

L108 ANSWER 7 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 1988-273888 [39] WPIX
DNN N1988-208019 DNC C1988-121835
TI Base for cell cultivation - is prepd. from at least one of **sugar**, protein, lipid and/or complex cpd. such as glyco protein.
DC A97 B04 D16 D22 P73
PA (SUME) SUMITOMO ELECTRIC IND CO
CYC 1
PI JP 63198978 A 19880817 (198839)* 9p
ADT JP 63198978 A JP 1987-32230 19870213
PRAI JP 1987-32230 19870213
IC B32B005-18; B32B009-00; C08J007-00; **C12M003-00**; **C12N005-02**; C12N011-02
AB JP 63198978 A UPAB: 19930923
A base is prepd. by (a) coating the stratified **membrane** of monomolecular films on the high molecular base, whose surface is treated and (b) carrying at least one of the substance of **sugar**, protein, lipid and/or the complex cpd. such as glycoprotein on the stratified **membrane**.

It is pref. to use high molecular base, whose surface is treated by plasma, sputtering, UV-ray, electronic ray, gamma-ray, ion, ozone or chemicals. Porous high molecular base and hollow fibre-form high molecular base are pref. The surface of the stratified **membrane** is pref. partly treated by UV-ray, electronic ray or ion. It is pref. to carry glycoprotein, etc. on stratified **membrane** partly in fretwork, striped pattern or polka dots.

USE/ADVANTAGE - Surface-treated, high molecular base has good adhesive property to stratified **membrane**, and stratified **membrane** is regulated to such a structure that it might be suitable for adhering cells. The stratified **membrane** carries glycoprotein, etc. strongly and glycoprotein, etc. has good adhesive property to cells and prolonging property and multiplying property of cells. Thus it can be used for culturing the cells producing useful substances such as hormone and it can also be used as artificial organ. 0/1
FS CPI GMPI
FA AB
MC CPI: A11-C04B2; A11-C04D; A11-C04E; A12-S05A; A12-V02; A12-W11L; B04-B01B; B04-B02D; B04-B04A; **B04-C03**; B04-D01; B11-A; D05-C; D05-H02; **D05-H10**; D09-C01C

L108 ANSWER 8 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 1988-268194 [38] WPIX
DNC C1988-119501
TI Base for cell culture with adhesive properties - comprises porous or hollow fibrous high mol. wt. polymer with ozone-treated surface supporting e.g. **sugar** or protein.
DC A96 B04 D16
PA (SUME) SUMITOMO ELECTRIC IND CO
CYC 1
PI JP 63196277 A 19880815 (198838)* 6p
ADT JP 63196277 A JP 1987-29007 19870210
PRAI JP 1987-29007 19870210
IC **C12M003-00**; **C12N005-02**; C12N011-08
AB JP 63196277 A UPAB: 19930923
The base is composed of a porous or hollow fibres of high mol. wt. polymer surface treated with ozone and which supports partially one or more of **sugar**, protein, lipid or a mixt. of these in the form of stripe, lattice, or polka dot.

The high mol. wt. polymer includes polymers of series of olefins, fluorine polymers, styrene, acryl, vinyl, polyester, epoxy, cellulose, or

silicone or a mixt. of these. These polymers may take any form, e.g., film, tube, hollow fibre, particles, pref. hollow fibre with inner dias. of 50-1,000 microns for high density cultivation or particles of dia. of 100-300 microns. Ozone treatment is performed by the introduction of zone produced by conventional generator at a level of 0.2-10 v/v% pref. 0.3-3 v/v%, then the treated base is washed with water and dried. **Sugars** , glycoproteins, proteins, lipids, lipoproteins or a mixt. of these may be coated by dipping or painting in a mono or polymolecular layer.

USE/ADVANTAGE - The base is used for cultivation of animal cells for the prodn. of biologically active substance substances, e.g., vaccine, hormone, interferon. The base has satisfactory adhesive property with animal cells for the control of cultivation.

0/1

FS CPI
FA AB
MC CPI: A12-S05A; A12-W11L; B02-V02; B02-V03; B04-B02D; B04-B04A3; B04-C03B; B11-A; D05-C; D05-H01; D05-H07; **D05-H08**

=> d l109 all abeq tech abex tot

L109 ANSWER 1 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2003-092922 [08] WPIX
DNC C2003-023179
TI Solid support for e.g., combinatorial library synthesis, comprises ligand(s) immobilized to a **polyol** (allyl carbonate) polymer solid support.
DC A26 A89 B04 D16
IN DUMAS, D P
PA (DUMA-I) DUMAS D P
CYC 100
PI WO 2002081086 A1 20021017 (200308)* EN 51p B01L003-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003013188 A1 20030116 (200308) C12M003-00 <--
ADT WO 2002081086 A1 WO 2002-US11249 20020408; US 2003013188 A1 Provisional US 2001-282691P 20010409, US 2002-118556 20020408
PRAI US 2001-282691P 20010409; US 2002-118556 20020408
IC ICM B01L003-00; **C12M003-00**
ICS **C12M001-00; C12M001-22; C12M001-24; C12M001-34; C12M001-36**
AB WO 200281086 A UPAB: 20030204
NOVELTY - A solid support (I) comprises ligand(s) immobilized to a **polyol** (allyl carbonate) polymer solid support.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a multi-well plate comprising (I) having several wells;

(2) a tissue culture vessel comprising a **polyol** (allyl carbonate) polymer;

(3) generating a solid support by immobilizing ligand(s) to a **polyol** (allyl carbonate) polymer solid support;

(4) attaching a chemical compound to a solid support by contacting the **polyol** (allyl carbonate) polymer solid support with a chemical group; and

(5) a microfluidic device comprising (I) having one or more microchannels and wells.

USE - The solid support can be in the form of a multi-well plate, a tissue culture vessel or a microfluidic device. It can be also be in the

form of a bead, fiber, flat surface, molded device, machined device, or mass spectrometry sample holder (claimed). The solid support is used for chemical storage, chemical synthesis, combinatorial library synthesis, analytical devices, diagnostic devices, and tissue culture applications.

ADVANTAGE - The solid support has high clarity, low intrinsic fluorescence, and resistance to a variety of chemical solvents. It can be chemically modified to allow attachment of a chemical group. It allows highly efficient solid phase synthesis.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A04-A03; A04-B09; A12-W11L; **B04-C03**; B04-E01; B04-N04; B10-A11B; B11-C06; B11-C08E6; B11-C09; B12-K04; D05-H09; **D05-H10**

TECH UPTX: 20030204

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Vessel: The tissue culture vessel is a flask, tube, plate, or microfluidic device, preferably a multi-well plate. The surface of the tissue culture cell is modified for attachment of a cell.

Preferred Device: The microchannels of (5) are formed by laser ablation, or by molding or casting. One or more ligands are immobilized in the microchannels. The device is modified to contain a chemical functional group that is an amine, alkyl, hydroxyl, aromatic, or a carboxylate group.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The ligands comprise a nucleic acid or a polypeptide. The **polyol** (allyl carbonate) polymer is diethylene **glycol** bis(allyl carbonate) or a copolymer comprising greater than 10 % diethylene **glycol** bis(allyl carbonate). The polymer is generated by polymerizing a prepolymer of **polyol** (allyl carbonate).

Preparation: The method of (4) further comprises contacting the solid support with a second chemical group, and optionally repeated the contacting.

L109 ANSWER 2 OF 8 WPIX (C) 2003 THOMSON DERWENT

AN 2002-723156 [78] WPIX

DNN N2002-570259 DNC C2002-204650

TI Sample carrier for analysis of chemical and biological samples has surface made from a polymer or polymer composite, at least one area of which has free binding positions with one or more functional groups.

DC A17 A89 B04 D16 S03

IN RAEDLER, U

PA (IBID-N) IBIDI GMBH

CYC 100

PI WO 2002063304 A2 20020815 (200278)* DE 19p G01N033-543

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

DE 10105711 A1 20020905 (200278) G01N033-544

ADT WO 2002063304 A2 WO 2002-EP1343 20020208; DE 10105711 A1 DE 2001-10105711 20010208

PRAI DE 2001-10105711 20010208

IC ICM G01N033-543; G01N033-544

ICS B01L003-00; **C12M001-42**; C12N011-00; G01N021-64

AB WO 200263304 A UPAB: 20021204

NOVELTY - Sample carrier for analysis of chemical and biological samples has a surface (2) made from polymer or a polymer composite. At least one area (4) of this has free binding positions with one or more functional groups.

USE - In analysis of pharmaceuticals, environmental samples, DNA,

RNA, proteins, antigens, antibodies or cells and cell fragments.
ADVANTAGE - The carrier has optical properties which are suitable for various optical analysis methods.
DESCRIPTION OF DRAWING(S) - The drawing shows a schematic view of the carrier for analysis of chemical and biological samples.
Polymer coating 2
Zones with different functionality 4, 4', 4,4'
Dwg.1/2

FS CPI EPI
FA AB; GI; DCN
MC CPI: A12-L04; A12-V03C2; A12-W11L; B04-C01; **B04-C03**; B04-E01; B04-F01; B04-G01; B04-N04; B11-C08E; B11-C08F2; B11-C08F4; B11-C08G; B12-K04E; D05-H09; **D05-H10**; D05-H12; D05-H18; D05-J
EPI: S03-E04X; S03-E14A1; S03-E14H
TECH UPTX: 20021204
TECHNOLOGY FOCUS - POLYMERS - Preferred Polymers: The polymer is a cyclic olefin polymer, norbornene polymer and/or cyclic olefin copolymer and/or polypropylene.
ABEX UPTX: 20021204
EXAMPLE - In an EMBODIMENT the functional groups are carboxyl, amino, thiol, hydroxy, aldehyde, acid halide or polyethylene **glycol** groups. additional reactive groups may be bound to these, especially iminodiacetic acid groups, nitrilotriacetic acid derivatives or biotin derivatives or metals. The polymer coating may have several zones (4, 4', 4,4') with different functionality. The polymer is transparent, especially to UV, and has no birefringence or autofluorescence properties.

L109 ANSWER 3 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2002-643428 [69] WPIX
DNN N2002-508602 DNC C2002-181748
TI Manufacture of biochips with immobilization reinforcing liquid and conditioned specimen on a substrate to form a plurality of capture spots arranged for specific reaction to obtain information on structure or function of a subject.
DC B04 D16 S03
IN HIROTA, T; OHNISHI, T; TAKEUCHI, Y; YAMADA, K; YAMADA, S
PA (NIGA) NGK INSULATORS LTD
CYC 9
PI WO 2002063310 A1 20020815 (200269)* JA 71p G01N037-00
RW: CH DE FI FR GB IT NL
W: JP
US 2002155481 A1 20021024 (200273) C12Q001-68
ADT WO 2002063310 A1 WO 2002-JP1011 20020207; US 2002155481 A1 US 2002-68292 20020206
PRAI JP 2001-32829 20010208
IC ICM C12Q001-68; G01N037-00
ICS **C12M001-34**; G01N033-53; G01N033-542
AB WO 200263310 A UPAB: 20021026
NOVELTY - Biochips with a plurality of capture spots arranged on the substrate (10) can be produced by feeding onto such substrate a plurality kinds of captures reacting specifically to a subject and used to obtain information on the structure and function of the subject, in which some of the spots at various positions are formed with a first substance to support immobilization onto the substrate with captures.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for manufacturing a biochip by feeding an immobilization reinforcing liquid (16) onto a substrate (10) together with a specimen (14) to form capture spots in multiple arrays when liquid specimens containing captures and without are respectively supplied, and optionally with formation of the first and second substances at some of the spots to support or inhibit immobilization onto the substrate with captures.
USE - The biochips are formed with a plurality of capture spots arranged for specific reaction to obtain information on structure or

function of subject, which are applicable in gene and protein analysis as well as diagnosis of diseases.

ADVANTAGE - The spots can be arranged at high density, e.g. microspots like DNA fragments in DNA microarray form.

DESCRIPTION OF DRAWING(S) - The process for integration of specimen and immobilization reinforcing liquid. (Drawing includes non-English language text).

Substrate 10

Poly-L-lysine 12

Specimen 14

Immobilization reinforcing liquid 16

Dwg.4C/16

FS CPI EPI

FA AB; GI; DCN

MC CPI: B04-B04C; **B04-C03**; B04-E01; B04-G01; B04-N04; B11-C08E6; B11-C08F2; B11-C08F4; B12-K04A; B12-K04E; B12-K04F; D05-H09; **D05-H10**; D05-H12

EPI: S03-E03C1; S03-E14H

TECH UPTX: 20021026

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Biochips: The first substance for supporting immobilization is the liquid specimen (14) without captures, and the immobilization (reinforcing) liquid (16) is for (reinforcing) immobilization of the captures onto the substrate. Such first substance is formed to support immobilization onto the substrate with captures at some of the spots are formed on the substrate (10), and the positions other than those with the spots are formed with the second substance that inhibits immobilization onto the substrate with some captures and to prevent adhesion of the subject onto the substrate.. The first substance is formed on the whole of the substrate (10) and the second substance on the first substance to partially form at places other than those formed with the spots.

Preferred Methods: The capture-containing liquid specimen (14), or that without, is fed by the inkjet method, and the liquid specimen without captures can be fed by screen-printing method as well. The liquid specimen without captures can be the immobilization liquid or/and immobilization reinforcing liquid for (reinforcing) immobilization onto the substrate (10) with captures. The immobilization liquid or immobilization reinforcing liquid (16) is optionally the liquid specimen containing captures or its mixture as a liquid providing immobilization or reinforcing immobilization. After feeding the capture-containing liquid specimen (14) to the substrate (10), a part of the immobilization or immobilization reinforcing liquid (16) is fed to the specimen, and then the capture-containing liquid specimen is fed to the supplied part of the immobilization (reinforcing) liquid; or both immobilization and immobilization reinforcing liquids can be fed almost simultaneously as the liquid specimen containing captures.

The substrate (10) can be a set of tools to which the liquid specimens containing captures or without are fed for immobilization, particularly to various regions to form almost round spots, especially with more of the liquid specimen without captures in not less than 2 as many regions. The first substance is formed on some of the (predetermined) spots, while the second substance on the other in the substrate (10). Such second substance can particularly inhibit immobilization onto the substrate with captures and prevent adhesion of the subject onto the substrate, which can be supplied by the inkjetting, screen-printing or dipping method. A resist is particularly formed on the location of the spot on which the first substance is formed on the substrate (10), with the second substance formed on the whole of the resist by dipping, and after lifting off the resist, the second substance is formed on locations other than those formed with the spots.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Methods: The captures can be nucleic acids, e.g. DNAs, cDNAs, RNAs or antisense RNAs, synthetic DNAs or RNAs, their fragments or amplification products; or can be proteins

like antigens, antibodies, lectins, adhesins, receptors of physiologically-active substances and peptides. The immobilization liquid is particularly a chemical solution containing positive charge for immobilization of the captures by ionic bond, which can be silane coupling agent such as gamma-aminopropyltriethoxysilane, poly-L-lysine or polyalkylene. This chemical substance in the immobilization solution is particularly for chemical modification of the substrate surface (10), and the captures are modified by reacting with the introduced functional group on such substrate surface to form covalent bond between the capture and substrate for immobilization.
Such chemical reaction can be that between amino and aldehyde groups, amino and N-hydroxysuccinimide groups, amino and carboxyl groups, amino and epoxy groups, or thiol and epoxy groups. The immobilization liquid is avidin, streptoavidin, protamine or histone; or a solution containing phenyl, alkyl or other hydrophobic groups. The immobilization reinforcing liquid (16) is a water-retaining substance including cholaminic acid, hyaluronic acid or their mixture; or a polymer e.g. acidic polymer of CM-cellulose, nitrocellulose, polyacrylic acid or alginic acid, or basic polymer of polyethylene imine or polyacrylamide, neutral polymer of methylcellulose, polyethylene **glycol** or polypropylene **glycol**, or protein like BSA (bovine serum albumin), ovalbumin, lysozyme. The first substance particularly contains a mixture of gamma-aminopropyltriethoxysilane/glutaraldehyde, gamma-aminopropyltriethoxysilane/succinimic anhydride/N-hydroxysuccinimide, or gamma-aminopropyltriethoxysilane/succinic anhydride, epichlorohydrin, or bisoxysliane, whereas the second substance contains at least amino acids, amino-containing Tris, ethanolamine, thiol-containing cysteine, glutathione, or thioburaicol (sic).
When the first substance is a chemical substance for modifying the substrate surface by supporting immobilization onto the substrate (10) with captures through affinity binding, the second substance is a substance for affinity binding with the chemical substance. So, the first substance can contain avidin, streptoavidin, protamine, histone, biotin, antigen, antibody-binding protein, or/and antibody, while the second substance contains at least avidin, streptoavidin, biotin, nucleic acid, antigen, antibody-binding protein or/and antibody. The first substance is especially a chemical substance for substrate-surface modification that contains hydrophobic groups like styryl, phenyl and/or alkyl, which can support immobilization onto the substrate (10) with captures by hydrophobic bond, and the second substance contains at least some amphoteric substances; particularly the first substance containing polystyrene or/and alkylbenzene, and the second substance containing gelatin or/and casein. Such second substance can be a water-repelling substance e.g. silicone or/and fluorine-containing material

ABEX UPTX: 20021026

EXAMPLE - A biochip was assembled as specified for detecting nucleic acids or proteins.

L109 ANSWER 4 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2002-074889 [10] WPIX
DNC C2002-022197
TI New electrophysiological assay system and methods, used to determine a compound's acute and chronic effect on cellular function in living cells.
DC A85 B04 D16 L03
IN HICKMAN, J J
PA (HICK-I) HICKMAN J J
CYC 92
PI WO 2000071742 A2 20001130 (200210)* EN 65p C12Q001-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK

SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
EP 1180162 A2 20020220 (200221) EN C12Q001-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 2000051508 A 20001212 (200252) C12Q001-00
JP 2003500065 W 20030107 (200314) 98p C12M001-34 <--

ADT WO 2000071742 A2 WO 2000-US13966 20000522; EP 1180162 A2 EP 2000-936147 20000522, WO 2000-US13966 20000522; AU 2000051508 A AU 2000-51508 20000522; JP 2003500065 W JP 2000-620119 20000522, WO 2000-US13966 20000522

FDT EP 1180162 A2 Based on WO 200071742; AU 2000051508 A Based on WO 200071742; JP 2003500065 W Based on WO 200071742

PRAI US 1999-135275P 19990521

IC ICM **C12M001-34**; C12Q001-00
ICS C12Q001-02

AB WO 200071742 A UPAB: 20020213
NOVELTY - A system capable of identifying one or more ion channels of a cell, which channels are affected by a test substance, comprising a device and accompanying software, is new.

DETAILED DESCRIPTION - A system (I) capable of identifying one or more ion channels of a cell, which channels are affected by a test substance, comprising a device and accompanying software, in which the device comprises:

(a) a solid state microelectrode;

(b) a cell culture comprising one or more electrically active cells having a cell **membrane** including one or more ion channels, where the cells are capable of providing a measurable action potential that exhibits one or more perceptible characteristics; and

(c) an intervening layer which comprises;

(i) a surface modifying agent ; and

(ii) is positioned between the microelectrode and the cells of the cell culture, such that a high independance seal is provided in the vicinity;

and in which the accompanying software comprises instructions that can be implemented by a computer and which are capable of relating changes in the characteristics exhibited by the action potential to one or more of the ion channels of one or more of the cells upon exposure to the test substance.

INDEPENDANT CLAIMS are also included for the following:

(1) a computer readable medium encoding a program that includes instructions for execution by a computer, which comprises data processing steps that relate changes in one or more characteristics exhibited by an observed action potential to one or more ion channels of the cells in the culture upon exposure to the test substance.

(2) a system for determining one or more potential functions of an isolated nucleic acid or its expression product using (I).

USE - The system is useful for determining a compound's acute and chronic effect on cellular functions in living cells.

Dwg.0/11

FS CPI
FA AB; DCN
MC CPI: A12-E14; A12-L04B; A12-V03C2; A12-W11L; B04-C02A; B04-C02A1; B04-C02C; **B04-C03**; B04-E02; B04-E03; B04-F0200E; B05-A01B; B05-A02; B05-B02B; B05-B02C; B06-F03; B11-C08B; B11-C08E1; B11-C10A; B12-K04E; **D05-H08**; D05-H09; **D05-H10**; D05-H14B2; L03-H03A

TECH UPTX: 20020213
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: No suitable data given.
Preferred System: Characteristics exhibited by the action potential are manifested in a waveform such as after potential, time to cessation of activity, frequency, amplitude, shape, shape, spike rate, time constant or in the temporal description of the cation potential.
Data processing instructions are capable of receiving input data through

sodium channels, potassium channels, calcium channels or combinations of them and includes a temporal analysis of the action potential or the changes observed by them, is capable of providing an output suggestive of the involvement of one or more cellular pathways or receptors of interest, and is capable of determining a mode of action of a test substance based on the one or more cellular pathways or receptors of interest involved. The microelectrode is preferably planar or flexible and even more preferably is a field effect transducer.
The insulator is selected from silicon, modified silicon dioxide, silicon nitride, silicon carbide, germanium, silica, gallium, arsenide, epoxy resin, polystyrene, polysulfone, alumina, silicone, fluoropolymer, polyester, acrylic polymers, polylactate or their combinations.
The cell culture comprises a stem cell, a transformed stem cell, their respective progeny or their combinations and where the stem cell is exposed to a differentiating factor, the cells being transfected with endogenous or exogenous nucleic acid and coated with a polymer comprising cellulose, methylcellulose and dextran.
The surface modifying agent comprises a self-assembling monolayer which further comprises a silane, a thiol, a polyelectrolyte or similar molecules or their combinations.
The system further comprises a detector circuit.
The software comprises instructions for manipulating one or more system parameters to alter one or more conditions of a given experiment, for interpreting the outcome of such manipulations, or for both where the manipulations include the addition or removal of a compound of interest to or from the cell culture and includes instructions for a feedback loop.
Preferred Layer: The intervening layer further comprises cell anchorage molecules which comprise antibodies, antigens, receptor ligands, receptors, lectins, carbohydrates, enzymes, enzyme inhibitors, biotin, avidin, streptavidin, cadherins, RGD-type peptides, integrins, modified lipids or their combinations. It further comprises a high viscosity mixture consisting of alcohols, ethers, esters, ketones, amides, **glycols**, amino acids, saccharides, carboxymethylsaccharides, carboxyethylsaccharides, aminosaccharides, acetylaminosaccharides and their polymers or combinations and may be characterized as a repulsive or an attractive layer.
Preferred cell: The cell is preferably a neuronal or cardiac cell even more preferably is a hippocampal cell.
Preferred Substance: The test substance comprises a toxin, a drug, a pathogen, a neurotransmitter, a nerve agent a gene or a gene product or their mixtures or more preferably is a nutritive material or a cell modulator.
Preferred Medium: The computer readable medium preferably comprises a deconvolution step in which the changes in the characteristics exhibited by the observed action potential are compared with stored information from past observations allowing the computer to attribute the changes to the ion channels of the cells. The data processing steps do not include spectral analysis which, makes use of a Fourier transform.

ABEX UPTX: 20020213

EXAMPLE - Primary hippocampal neurons are grown under highly standardized conditions. Cells used are: Young control neurones (YC) isolated from fresh cadavers of adolescents or young adults (15-30 years); Age-matched control neurons (AC) isolated from fresh cadavers of elderly humans (60-80 years); and Alzheimer's Disease neurons (AD) isolated from fresh cadavers of elderly humans (60-80 years) with clinically diagnosed Alzheimer's Disease.
Cells were seeded onto microelectrode arrays in enriched culture medium and used when impedance measurements indicate establishment of a high impedance seal between at least one neuron and the substratum.
Electrophysiological measurements are performed at room temperature (21-23 degrees C) or, in other cases , as a function of temperature. Before recordings, culture medium is replaced with the following solution: 115mM NaCl, 40 mM KCL, 2mM CaCl2 , 1mM MgCl2,10mM HEPES (NaCl) pH=7.4, or

alternatively fresh medium with selected neurotransmitter. Multiple types of sodium , calcium and potassium channels within each cell and cell type are distinguished and recorded based on parameters of each channel, including conductance and current. Differences in ion channel properties between cells of different lineage are also recorded. In other measurements , the response of cells to a battery of neurotransmitter agonists is recorded, where the neurotransmitters include glutamate, carbachol, gamma amino butyric acid (GABA) and serotonin. Specific but partial attenuation of ion channels with graded doses of toxins including TEA (K+channel), tetrodoxin (Na+channel) and amiloride (Ca2+ channel) are used in conjunction with deconvolution of the action potentials to determine the effect of model inhibitors. Additional agents and channel blockers were also used.

L109 ANSWER 5 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2001-611328 [70] WPIX
DNC C2001-182614
TI Association device for nucleic acid-based diagnostic test, isolation of nucleic acids, comprises oligonucleotide probe and solid substrate having support surface comprising association surface for linking probe to substrate.
DC A96 B04 D16
IN BELOSLUDTSEV, I Y; BELOSLUDTSEV, Y Y; HOGAN, M; IVERSON, B; POWDRILL, T
PA (GENO-N) GENOMETRIX GENOMIX INC
CYC 94
PI WO 2001066687 A1 20010913 (200170)* EN 101p C12M001-34 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000069393 A 20010917 (200204) C12M001-34 <--
ADT WO 2001066687 A1 WO 2000-US23438 20000824; AU 2000069393 A AU 2000-69393 20000824
FDT AU 2000069393 A Based on WO 200166687
PRAI US 2000-636268 20000810; US 2000-522240 20000309
IC ICM **C12M001-34**
ICS G01N033-00
AB WO 200166687 A UPAB: 20011129
NOVELTY - Association device comprises nucleic acid and polypeptide probes, or combinations of these, linked to porous solid substrate (SS). SS comprises a surface comprising an external substrate surface and several internal pores. The pore surfaces comprise an association surface (AS) which is charged with net positive or negative charge density where the pH is lower or higher than the pI of AS.

DETAILED DESCRIPTION - The device has many nucleic acid probes, polypeptide probes or their combinations linked to a porous SS which comprises a surface comprising an external substrate surface and several internal pores. The pores comprise a proximal end opening to the external surface to allow passage of fluid into a pore and the pore surfaces comprise AS. The distance between the nucleic acid probe or the polypeptide probe and the charged AS is not more than 100 Angstrom .

INDEPENDENT CLAIMS are also included for the following:

(1) making the above device, by contacting a biotinylated nucleic acid probe with streptavidin tetramer in an aqueous solution, applying the solution directly to clean porous polystyrene surface or its equivalent and incubating the probe-applied polystyrene in a humid environment for a time to allow stable absorption of the streptavidin to the polystyrene surface; and

(2) making a porous surface of an association device, by:

(a) co-polymerizing streptavidin and biotinylated nucleic acid probes into a mixture of acrylamide and bis-acrylamide or co-polymerizing

streptavidin into a mixture of acrylamide and bis-acrylamide, under conditions where a porous matrix polymerizes and after polymerization adding biotinylated nucleic acid probe to the polymerized porous matrix by perfusion; or

(b) contacting a porous silica matrix with a solution of activated silane by a gas phase or fluid phase deposition.

USE - The association/hybridization device is useful for associating a nucleic acid or a polypeptide in a sample to a nucleic acid or a polypeptide probe. The method comprises contacting a test sample with the device under conditions of pH higher or lower than the pI of AS, thereby inducing a net positive or negative charge density, respectively on AS. The desired pH is established by contacting the device with an aqueous solution buffered to obtain the desired pH. The nucleic acid or polypeptide not associated with the probe are washed with a buffered aqueous solution and the wash conditions induce or maintain a net positive or negative charge density on the surface of the device. The nucleic acid or polypeptide remaining associated with the probes after the washing are removed and the non-associated sample is then detected. The device is also useful for detecting a single base pair difference between a nucleic acid in a test sample and an oligonucleotide probe. The test sample is contacted with the device under conditions that induce the substrate surface or AS to have a net positive (cationic) charge density under no salt or low salt conditions and AS is altered to an anionic environment by changing the conditions to comprises a pH that induces a net negative charge density to AS, or a neutral charge density by coating AS with a neutral or anionic polymer composition. Test sample nucleic acid not associated with a probe is removed under the altered conditions and nucleic acid remaining hybridized to the nucleic acid probe is detected (all claimed).

The device finds application in nucleic acid-based diagnostic tests, isolation and purification of nucleic acids or polypeptides from a sample.

ADVANTAGE - The device can be used at any temperature and the kinetics of association between the oligonucleotide probe and the nucleic acid in the test sample are 10 fold more rapid than the kinetics of association under conditions when the substrate surface or AS has a neutral or net negative charge density. The device and the method can be used for association/hybridization of probes to target DNA or RNA at low bulk ion concentrations. This method is effective as the surface loading of cations on a solid support creates a hybridization surface that results in a high local cation density near the surface. The electrostatic field created on the surface of SS by AS enhances the selectivity of duplex binding due to the interaction between the mismatches in the target, the probe and the electrostatic field of the surface.

Dwg.0/18

FS CPI

FA AB; DCN

MC CPI: A04-C01; A04-D04A; A11-C04B2; A12-S04A3; A12-V03C2; B04-E01; B04-E05; B04-N04; B11-B; B11-C08E; B11-C08E5; B11-C09; B12-K04E; B12-K04F; D05-H09; **D05-H10**; D05-H12D1; D05-H13

TECH UPTX: 20011129

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Arrangement: The device further comprises an aqueous solution comprising a pH lower or higher than that of pI of AS, thereby inducing a net positive or negative charge density, respectively on AS. The net positive or negative charge density on AS induces a net positive or negative charge density in the pore space of the device and generates a thermodynamic partitioning equilibrium favorable to the movement of negatively or positively charged molecules, respectively into the pore space from the aqueous solution outside of the pores and favorable to the movement of charged molecules out of the pore space.

The thermodynamic equilibrium is favorable to the movement of negatively charged DNA, RNA or polypeptides. The positively charged AS comprises at least 1011 charges/mm2 or its charge equivalent.

Preferred Substrate: SS comprises a porous bead, a microsphere, **membrane**, microporous **membrane**, film, polytetrafluoroethylene filter, fiber, hollow fiber, fabric, polyacrylamide, polymethacylamide, methyl methacrylate, glycidyl methacrylate, dialkylaminoalkyl-(meth)acrylate, N,N-dialkylaminoalkyl(meth)acrylate, agarose, polyimid, controlled pore silica, glass, porous foam comprising poly(D,L glycolic-co-lactic acid) or poly(D,L-lactide-co-glycolide) (PLGA), porous ceramic, poly(**ethylene glycol terephthalate**) (PEGT) or poly(butylene terephthalate) (PBT), monodispersed carbon nanotube or its equivalent comprising patterned porous silicon, porous polystyrene, poly(styrene-divinylbenzene) (PS-DVB), plastic, plastic copolymer, polyvinyl, polypropylene, polyester, poly(vinyl alcohol) (PVA) hydrogel nanoparticle or their equivalents.

SS comprises several different nucleic acid probes arranged in spatially defined areas over the surface of the association device. The pores comprises a closed distal end and an open distal end which allows passage of fluid through the pore. Only the pore surfaces comprise AS.

The distance between the nucleic acid probe and charged surface is not more than 100 (preferably 20) Angstrom.

The nucleic acid or the polypeptide probe is 11-20 residues in length and are covalently attached to AS.

AS comprises streptavidin, imidazole, citrate, histidine or their derivatives linked to an oligonucleotide or polypeptide probe at a density of 1010 molecules/mm2. The internal pores comprise a diameter of 10-1000 Angstrom, preferably 500 Angstrom. AS comprises streptavidin, histidine or imidazole (or their derivative) and has a net positive charge density at pH lower than pH 5.5, 6.7 and 6, respectively and a net negative charge density at pH higher than the above pH values. AS comprises an amino acid or peptide linked to SS surface by its amino terminal end and an aminated oligonucleotide linked to the carboxy terminal end of the amino acid or peptide.

The peptide comprises: ((arg)n-pro)n-argn, ((arg)n-pro-gly)n-argn, or ((arg)n-gly-gly)n-argn

n = 2, 3, 4, 5 or 6.

A preferred peptide comprises: ((arg)5-pro)5-arg5,((arg)5-pro)4-arg5, ((arg)5-pro-gly)3-arg5, ((arg)5-pro-gly)4-arg5, ((arg)5-gly-gly)3-arg5 or ((arg)5-gly-gly)4-arg5.

Preferred Method: In (2), the mixture comprises 19% acrylamide and 1% bis-acrylamide. The final concentration of streptavidin is 10-6 M streptavidin tetramer.

ABEX UPTX: 20011129

WIDER DISCLOSURE - Also disclosed as new are kits comprising the device.

EXAMPLE - Microarrays were fabricated using biotin-modified oligonucleotide probes complexed with streptavidin (SA). SA was bound to the biotinylated probes, thus non-covalently attaching the probes to the solid support surface of the association device. At low salt and pH 5, where SA has a positive charge, duplex formation was 80 fold faster then seen under standard conditions, where SA was neutral or anionic. Tunable surface DNA microarrays were fabricated by modifying oligonucleotides with terminal biotin. Biotinylated probes were then complexed in solution with a SA tetramer at a 4/1 ratio of oligomer or tetramer. This protein-DNA complex was then printed directly onto clean polystyrene and allowed to link to the surface. As a representative DNA hybridization model, a 157 bp PCR fragment of the human k-ras oncogene was used. Oligonucleotides complementary to codon 12 mutations were designed to serve as capture probes on the array. Cell-lined derived PCR k-ras amplicon targets complementary to capture probes were used. K-ras amplicons were amplified by PCR using primers for k-ras amplicons labeled with digoxigenin at their 5' ends during synthesis. The kinetics of target k-ras amplicon (the test sample) hybridization to the probe (immobilized to the SA surface of the device) under standard high salt, high pH conditions was compared to hybridization under low salt, low pH conditions. High salt, high pH

prehybridization solution contained 150 mM sodium citrate, 5XDenhardt's solution, pH 8.0 and this was applied to the array for 10 minutes. It was vacuumed off and high salt, high pH hybridization solution (1 nM amplicon, 0.1 microM chaperone, 150 mM sodium citrate with respect to sodium 5X Denhardt's solution, pH 8.0) was applied to the array. After hybridization, the array was washed two times in 100 mM sodium citrate. Low salt, low pH prehybridization solution contained 0.2% Tween 20 in 5X Denhardt's solution. The low salt, low pH hybridization solution (1 nM of amplicon in 2 mM sodium phosphate, containing 0.1% Tween 20 at pH 5.0) was applied to the array. The digoxigenin-labeled amplicon was detected using anti-digoxigenin antibody linked to alkaline phosphatase and by an enzyme linked fluorescent substrate. Hybridization kinetics for a 1 nM solution of the wild type (WT) k-ras amplicon was a simple exponential rise to equilibrium, with a half time of approximately40 minutes at standard high salt, high pH conditions and less than 30 seconds for low salt, pH condition. Thus the observed hybridization rate enhancement with low ionic strength and low pH conditions was at least 80 fold.

L109 ANSWER 6 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2001-308000 [32] WPIX
DNC C2001-095098
TI Magnetic nanoparticles carrying specific binding agent reactive with intracellular molecule, useful for separating cells, particularly cancerous, and biomolecules.
DC A96 B04 B05 D16
IN BUSKE, N; CLEMENT, J; DIMITRI BERKOV, M B K; GANSAU, C; GOERNERT, P; HOEFFKEN, K; KLICHE, K; KOBER, T; SCHNABELRAUCH, M; VOGT, S; WAGNER, K; BAHR, M K; BERKOV, D
PA (BIOM-N) BIOMEDICAL APHERESE SYSTEME GMBH; (TRID-N) TRIDELTA BIOMEDICAL GMBH; (TRID-N) TRIDELTA BIO MEDICAL GMBH
CYC 95
PI WO 2001019405 A2 20010322 (200132)* DE 31p A61K047-48
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
DE 10046508 A1 20010405 (200132) A61K038-17
AU 2001016943 A 20010417 (200140) A61K047-48
EP 1216060 A2 20020626 (200249) DE A61K047-48
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
BR 2000014252 A 20021119 (200305) A61K047-48
CN 1379687 A 20021113 (200317) A61K047-48
JP 2003509034 W 20030311 (200319) 27p C12M001-00 <--
ADT WO 2001019405 A2 WO 2000-EP9004 20000914; DE 10046508 A1 DE 2000-10046508 20000914; AU 2001016943 A AU 2001-16943 20000914; EP 1216060 A2 EP 2000-979466 20000914, WO 2000-EP9004 20000914; BR 2000014252 A BR 2000-14252 20000914, WO 2000-EP9004 20000914; CN 1379687 A CN 2000-813707 20000914; JP 2003509034 W WO 2000-EP9004 20000914, JP 2001-523036 20000914
FDT AU 2001016943 A Based on WO 200119405; EP 1216060 A2 Based on WO 200119405; BR 2000014252 A Based on WO 200119405; JP 2003509034 W Based on WO 200119405
PRAI DE 1999-19944971 19990914
IC ICM A61K038-17; A61K047-48; C12M001-00
ICS A61K009-51; A61K031-711; A61K049-00; G01N033-48; G01N033-536; G01N033-553
ICA C07K017-14
AB WO 200119405 A UPAB: 20010611
NOVELTY - Magnetic nanoparticles (A) with biochemical activity comprises a magnetic core particle (I) and an attached covering layer (C), and includes a group Z, i.e. nucleic acid, protein and/or peptide (or their

derivatives), having at least one structure that binds specifically with a binding domain in an intracellular biomolecule.

DETAILED DESCRIPTION - Magnetic nanoparticle (A) with biochemical activity comprises a magnetic core particle (I) and an attached covering layer (C). (A) comprise a compound of formula M-S-L-Z.

Z = nucleic acid, protein and/or peptide (or their derivatives), having at least one structure that binds specifically with a binding domain in an intracellular biomolecule;

M = magnetic core;

S = biocompatible substrate;

L = linker.

INDEPENDENT CLAIMS are also included for the following:

(a) dispersion of (A) in a carrier liquid;

(b) biochemically active compound of formula S-L-Z (II);

(c) methods for preparing (A); and

(d) method for preparing (II).

USE - (A) are used to separate (i) cells, particularly malignant cells, but also healthy (e.g. embryonic) cells having a cell-specific gene expression pattern or (ii) intracellular biomolecules, particularly for molecular diagnosis of altered gene structures, especially precise identification of the breakpoint in the Philadelphia chromosome present in patients with chronic myeloid leukemia, but also solid tumors of breast and colon.

ADVANTAGE - (A) can penetrate cell **membranes** and bind very specifically to intracellular biomolecular targets, resulting in particle agglomeration and allowing separation of target cells in a magnetic field (contrast known methods of selection based on surface markers). They have high biocompatibility.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A12-E08; A12-L04; A12-V03C2; A12-W11L; B04-B01B; B04-B03C; B04-C02; B04-C02X; **B04-C03**; B04-E01; B04-F01; B04-N01; B04-N04; B04-N05; B04-N06; B05-A03A; B05-A03B; B12-K04A1; D05-H09; **D05-H10**; D05-H12; D05-H13

TECH UPTX: 20010611

TECHNOLOGY FOCUS - BIOLOGY - Preferred Materials: S is a poly- or oligo-saccharide or derivatives, e.g. (carboxymethyl)dextran or alginate; a protein or peptide (e.g. albumin); a synthetic polymer; or a bifunctional carboxylic acid (e.g. mercaptosuccinic or a hydroxycarboxylic acid). L is the residue of e.g. a poly- or di-carboxylic acid, diamine, amino acid, (lipo)protein, lectin, **sugar**, nucleic acid etc. It contains at least two, same or different, reactive groups, e.g. formyl, carboxy, amino, isocyanate, hydroxy or maleimido.
Preferred Particles: The bond between M and S is covalent or electrostatic.
Preferred Composition: In (a), the carrier fluid is polar and/or non-polar, particularly water and/or water-soluble solvent, and the dispersion may include physiologically active additives.
Preferred Targets: (A) are particularly targeted to fusion regions of genes, especially gene rearrangements associated with leukemia, lymphoma or sarcoma, and Z is then designed to hybridize with a complementary sequence in the mRNA derived from the gene rearrangement.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: In (c), the core particles are produced conventionally (e.g. thermolysis of metal carbonyls in an organic phase) then reacted with (II). The cores may also be reacted sequentially with S and then L-Z, or with S, a divalent molecule to introduce L and then with Z. In (d), (II) are prepared by reacting L-Z with S.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Cores: These are of magnetite, maghemite, ferrites of formula M'OxFe2O3, cobalt, iron, nickel,

or iron carbide or nitride. They have diameter 2-100 nm.
M' = divalent metal, e.g. cobalt, manganese or iron;
N.B. x is not defined.

TECHNOLOGY FOCUS - POLYMERS - Suitable polymeric S are poly(ethylene **glycol**), poly(vinyl pyrrolidone), polyethyleneimine and polymethacrylates.

ABEX UPTX: 20010611
EXAMPLE - Conventionally prepared magnetite particles were coated with bovine albumin, then diluted 1:40 in water and treated with a solution (in pH 7 phosphate buffer) prepared from (i) 10 microg of the oligonucleotide 5'-amino-ACTGGCCGCTGAAGGGCTTCTGCGTCTCCA-OH that had been activated by reaction with succinic acid in presence of N-ethyl-N'-(3-dimethylaminopropyl) carbodiimide (EDAC) and (ii) 20 microg EDAC. After reaction for 24 hours at 5-10degreesC, the mixture was purified by dialysis.

L109 ANSWER 7 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2000-516094 [47] WPIX
DNC C2000-154055
TI DNA chip comprises solid carrier and oligonucleotide or polynucleotide, which is fixed to carrier in presence of hydrophilic polymer.
DC A96 B04 D16
IN HAKAMATA, M; KUHARA, S; MUTA, S; TASHIRO, K; TSUCHIYA, T
PA (FUJF) FUJI PHOTO FILM CO LTD; (HAKA-I) HAKAMATA M; (KUHA-I) KUHARA S; (MUTA-I) MUTA S; (TASH-I) TASHIRO K; (TSUC-I) TSUCHIYA T
CYC 27
PI EP 1026259 A1 20000809 (200047)* EN 14p C12Q001-68
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000295990 A 20001024 (200059) 9p C12N015-09
US 2002090640 A1 20020711 (200248) C12Q001-68
EP 1026259 B1 20021127 (200279) EN C12Q001-68
R: DE FR GB SE
DE 60000836 E 20030109 (200312) C12Q001-68
ADT EP 1026259 A1 EP 2000-102619 20000208; JP 2000295990 A JP 2000-22180 20000131; US 2002090640 A1 Div ex US 2000-499717 20000208, US 2002-53326 20020117; EP 1026259 B1 EP 2000-102619 20000208; DE 60000836 E DE 2000-600836 20000208, EP 2000-102619 20000208
FDT DE 60000836 E Based on EP 1026259
PRAI JP 1999-30429 19990208
IC ICM C12N015-09; C12Q001-68
ICS B05D003-00; **C12M001-00; C12M001-34**
AB EP 1026259 A UPAB: 20000925
NOVELTY - A DNA chip comprises a solid carrier and oligonucleotide or polynucleotide, which is fixed to the carrier in the presence of a hydrophilic polymer.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method of fixing an oligonucleotide or polynucleotide to a solid carrier which comprises spotting an aqueous solution containing the oligonucleotide or polynucleotide and a hydrophilic polymer onto the carrier; and
(2) a process for detecting a DNA fragment complementary to oligonucleotide or polynucleotide fixed to a DNA chip comprising:
(a) spotting an aqueous solution containing the DNA fragment labelled with a fluorescent moiety on the DNA chip, which comprises a solid carrier and oligonucleotide or polynucleotide which is fixed to the carrier in the presence of a hydrophilic polymer;
(b) incubating the spotted chip for performing hybridization between the oligonucleotide or polynucleotide and the complementary DNA fragment in the aqueous solution; and
(c) detecting the hybridized complementary fragment by fluorometry.
USE - The DNA chip is useful in gene analysis.

Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: A12-W11L; B04-B03C; B04-C02A2; **B04-C03**; B04-E01; B04-E05; B04-N02; B04-N04; B11-C08E5; B12-K04F; D05-H09; **D05-H10**; D05-H12; D05-H12D1; D05-H18B
TECH UPTX: 20000925
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: The oligonucleotide or polynucleotide is fixed to the carrier at one end portion. The solid carrier is coated with poly-L-lysine. The oligonucleotide or polynucleotide has a NH2 terminal and is fixed to the carrier at its NH2 terminal. The hydrophilic polymer is selected from poly(1,4-diazoniabicyclo(2.2.2)octane-1,4-diylmethylene-1,4-phenylenemethylene chloride), polyacrylamide, polyethylene **glycol**, poly(sodium acrylate), carboxymethylcellulose and albumin. The oligonucleotide or polynucleotide is known in its base sequence. The oligonucleotide or polynucleotide is a synthetically prepared product or a cleaved DNA fragment.
Preferred Methods: The method of (1) further comprises the steps of washing the spotted carrier and drying the washed carrier.

L109 ANSWER 8 OF 8 WPIX (C) 2003 THOMSON DERWENT
AN 2000-147218 [13] WPIX
CR 1996-393530 [39]; 1997-393702 [36]; 1998-457256 [39]; 1998-495982 [42]; 1999-204741 [17]; 2000-071650 [06]; 2001-225814 [23]; 2002-089133 [12]; 2002-105080 [14]
DNN N2000-417837 DNC C2000-168574
TI Biopolymeric composition for detecting analytes e.g. pathogens, proteins or enzymes, comprises biopolymeric material that changes color in presence of analyte.
DC A96 B04 D16 S03
IN CHARYCH, D H; JONAS, U
PA (REGC) UNIV CALIFORNIA
CYC 22
PI WO 9967423 A1 19991229 (200013)* EN 175p C12Q001-68
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9947047 A 20000110 (200025) C12Q001-68
EP 1112377 A1 20010704 (200138) EN C12Q001-68
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 748644 B 20020606 (200249) C12Q001-68
ADT WO 9967423 A1 WO 1999-US14029 19990622; AU 9947047 A AU 1999-47047 19990622; EP 1112377 A1 EP 1999-930522 19990622, WO 1999-US14029 19990622; AU 748644 B Div ex AU 1998-63434 19980302, AU 1999-47047 19990622
FDT AU 9947047 A Based on WO 9967423; EP 1112377 A1 Based on WO 9967423; AU 748644 B Div ex AU 742885, Previous Publ. AU 9947047, Based on WO 9967423
PRAI US 1999-337973 19990621; US 1998-90266P 19980622; US 1999-337973 19990621
IC ICM C12Q001-68
ICS C07H021-04; **C12M001-00**; C12N011-00; G01N033-53
AB WO 9967423 A UPAB: 20020919
NOVELTY - Composition (A) comprising biopolymeric material (I) that changes color in presence of an analyte (II). (I) consists of many polymerized self-assembling monomers (III) and at least one nucleic acid ligand (IV).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a device containing at least one immobilized (I), and
(2) method for detecting (II) from its ability to cause a color change in (I).
USE - The method is used to detect nucleic acids, enzymes, pathogens (especially viruses, bacteria, parasites or fungi), drugs, receptor ligands, antigens, ions, proteins, hormones, blood components, antibodies

or lectins, e.g. for diagnosis of pathogens or genetic diseases, but also more generally organic solvents (e.g. in pharmaceutical products, air or water samples) or other small organic molecules. It can also be used to identify enzyme inhibitors; to screen enzymes or other catalytic molecules for activity and in drug development (by detecting competitive inhibition of a natural binding event).

ADVANTAGE - (II) can be detected directly and rapidly, either with the naked eye (e.g. for home use) or instrumentally. The method can be made quantitative; is easily adapted to high throughput screening and vesicles based on (I) have excellent storage stability.

Dwg.0/50

FS CPI EPI

FA AB; DCN

MC CPI: A12-V03C2; B04-B04C; **B04-C03**; B04-E01; B04-E05; B04-F09; B04-F10; B04-F11; B04-G01; B04-J01; B04-L01; B04-N04; B11-C07B1; B12-K04; D05-H04; D05-H05; D05-H06; D05-H09; **D05-H10**

EPI: S03-E14H4

TECH UPTX: 20001114

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: (IV) have affinity for (II); are single-stranded and are covalently linked to (III), particularly through amino, thiol or aldehyde groups. (II) is:

(a) a nucleic acid (any type of single- or double-stranded RNA or DNA, characteristic of pathogens or genetic abnormalities);

(b) an enzyme (especially polymerase, nuclease, ligase, telomerase or transcription factor);

(c) a pathogen (especially a virus (specifically influenza, rubella, varicella zoster, hepatitis A or B, herpes simplex, polio, smallpox, human immune deficiency, vaccinia, rabies, Epstein-Barr, retro or rhino virus), bacteria, parasite or fungus);

(d) a drug;

(e) a receptor ligand;

(f) an antigen;

(g) an ion; a

(h) protein;

(i) a hormone;

(j) a blood component;

(k) an antibody or

(l) a lectin.

(III) are particularly diacetylene monomers, especially derivatized with sialic acid, lactose or amino acids, and are polymerized to poly(diacetylenes) by ultra-violet radiation. (II) may also be e.g. acetylenes, alkenes, thiophenes, imides or urethanes, and they may contain carboxy, hydroxy, amino, amino acid or hydrophobic head groups. (I) may also include:

(i) a dopant to improve some property such as colorimetric response, color, density, pH or temperature sensitivity, especially a surfactant, polysorbate, octoxynol, sodium dodecyl sulfate, polyethylene **glycol**, zwitterionic detergent, decylglucoside, deoxycholate, diacetylene derivative; phosphatidyl -choline, -serine, -inositol, -ethanolamine or -glycerolcholesterol; phosphatidic acid, phosphatidyl methanol, cardiolipin, ceramide, cholesterol, steroid, cerebroside, lysophosphatidyl choline, D-erythrosphingosine, sphingolmyelin, dodecyl phosphatidyl choline or N-biotinyl phosphatidylethanolamine; and/or

(ii) a non-nucleic acid ligand (especially a carbohydrate, protein, drug, chromophore, chelating compound, molecular recognition complex, ionic group, polymerizable group, linker group, electron donor or acceptor, hydrophobic group, receptor binding group, tri- or tetra- saccharide, ganglioside, sialic acid and/or antigen).

The dopant is present at 2-10 mole%. (I) is in the form of a film (e.g. Langmuir-Boldgett film); liposome; tubule; braided, lamellar, helical or fiber-like assembly; or solvated coil or rod. It may be immobilized on a support, e.g. polystyrene, polyethylene, poly(tetrafluoroethylene), mica, Sepharose, Sephadex, polyacrylonitrile, filters, glass, gold, silicon

chips or silica.
Preferred Device: The device carries a patterned array of nucleic acid assays for determination of many different hybridization reactions.

ABEX UPTX: 20001114

WIDER DISCLOSURE - Also disclosed are similar compositions in which the ligand is other than a nucleic acid.

SPECIFIC COMPOUNDS - (III) are 5,7-docosadiynoic; 5,7-pentacosadiynoic and/or 10,12-pentacosadiynoic acids.

EXAMPLE - Two 35-mer probes (designated RAR1034 and 1037; see US 5599662) were synthesized conventionally, derivatized with amino groups and reacted with N-hydroxysuccinimido-poly(diacetylene). The resulting biomolecules were immobilized in microwells then incubated with a polymerase chain reaction product prepared from a blood samples suspected of containing human immune deficiency virus -1 (HIV-1) DNA, using primers described in the same reference. After hybridization for 30 minutes at 40degreesC, presence of HIV-1 DNA was indicated by a visible color change, without the need for washing or addition of developing reagents.

=> d his

(FILE 'HOME' ENTERED AT 06:45:38 ON 26 MAR 2003)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 06:45:52 ON 26 MAR 2003
E POLYETHYLENETEREPHTHALATE/CN
E POLY(ETHYLENETEREPHTHALATE)/CN
E POLY(ETHYLENE TEREPHTHALATE)/CN
L1 1 S E3
L2 1 S E8
L3 1 S L1,L2
E C8H6O4/MF
L4 77 S E3 AND 46.150.18/RID
L5 4 S L4 AND 1 4 BENZENEDICARBOXYLIC
L6 1 S L5 NOT (RADICAL OR D/ELS OR 11C)
E C8H4CL2O2/MF
L7 27 S E3 AND 46.150.18/RID
L8 1 S L7 AND 1 4 BENZENEDICARBONYL
E ETHYLENEGLYCOL/CN
E ETHYLENE GLYCOL/CN
L9 1 S E3
E C2H4CL2/MF
L10 36 S E3
L11 12 S L10 AND 1 2 DICHLORO
E ETHANE, 1,2-DICHLORO-/CN
L12 1 S E3
L13 2 S L6,L8
L14 2 S L9,L12
SEL RN L13
L15 28106 S E1-E2/CRN
SEL RN L14
L16 31985 S E3-E4/CRN
L17 9630 S L15 AND L16
L18 6 S L17 AND PMS/CI AND 2/NC
L19 3 S L18 NOT (TRIMER OR DIMER OR MAN/CI)
L20 4 S L3,L19
L21 1 S SUCROSE/CN
L22 3 S 69257-56-3 OR 92240-93-2 OR 92184-34-4
L23 1 S 56086-34-1
L24 3 S L21-L23 AND SUCROSE
L25 2 S L24 NOT ISOSUCROSE

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                SEL RN
L26          1706 S E5-E6/CRN
                E TRIS(HYDROXYMETHYL)AMINOMETHANE/CN
L27             1 S E3
                SEL RN
L28           942 S E1/CRN

     FILE 'HCAPLUS' ENTERED AT 06:56:08 ON 26 MAR 2003
L29            35 S ENGLEBRETH?(S)HOLM?(S)SWARM?
                E MEMBRANE/CT
L30         32694 S E3
                E E69+ALL
L31         32694 S E1
L32        157595 S E1+NT
L33           712 S L31,L32 (L) EXTRACELL?
                E EXTRACELLULAR MATRIX/CT
                E E3+ALL
L34         11032 S E14,E13+NT
L35            24 S L29 AND L30-L34
L36            17 S L29 AND EXTRACELL?(L) MATRIX
L37            25 S L29 AND ?MEMBRAN?
L38         60050 S L20
L39         55688 S POLYETHYLENETEREPHTHAL? OR POLY()(ETHYLENETEREPHTHAL? OR ETHY
L40         45726 S PET
L41           147 S POLY OXY 1 2 ETHANEDIYLOXYCARBONYL 1 4 PHENYLENECARBONYL
L42          1059 S DIMETHYL TEREPHTHALATE ETHYLENE GLYCOL COPOLYMER
L43          5617 S MELINEX OR MYLAR OR LUMIRROR OR PA 200
L44          3741 S (ETHYLENE GLYCOL OR ETHYLENEGLYCOL)()(TEREPHTHALIC ACID OR TE
L45             1 S L29 AND L38-L44
L46             1 S L29 AND (POLYOL OR POLYHYDRIC (L) ALCOHOL)
L47             2 S L29 AND (L27 OR BUFFER? OR TRIS HYDROXYMETHYL AMINOMETHANE)
L48             2 S L29 AND (L25 OR L20 OR SUCROSE)
L49             3 S L45-L48
L50             3 S L49 AND L35-L37
                SEL DN AN 1
L51             1 S E1-E3 AND L50
L52             1 S L29 AND COAT?/SC,SX,CW
L53             1 S L29 AND COAT?
L54             1 S L51-L53
                E MANNUZZA F/AU
L55            10 S E4-E6
                E FLAHERTY P/AU
L56             4 S E4,E12,E13
                E ILLSLEY S/AU
L57             1 S E4
                E ILSLEY S/AU
L58             4 S E3,E4
                E KRAMER M/AU
L59           287 S E3,E16
                E KRAMER MARTIN/AU
L60            36 S E3,E5
                E BECTON/PA,CS
L61          1649 S (BECTON? OR DICKINSON?)/PA,CS
L62             1 S L29 AND L55-L61
L63             1 S L54,L62
L64             4 S L29 AND (BIOCHEM?(L)METHOD?)/SC,SX
L65             4 S L63,L64
L66            31 S L29 NOT L65
L67             1 S L29 AND COAT?/SC,SX,CW,BI
L68             4 S L65,L67
L69             0 S L29 AND ?POLYM?
                E COATING/CT
                E E11+ALL
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L70             1 S L29 AND E3,E2+NT
                  E E116+ALL
L71             1 S L29 AND E7+NT
L72             4 S L68,L70,L71
                  E SEAL/CT
                  E E21+ALL
L73             1 S L29 AND E1
                  E E8+ALL
L74             0 S L29 AND E3,E4,E2+NT
L75             4 S L72,L73

     FILE 'HCAPLUS' ENTERED AT 07:12:37 ON 26 MAR 2003
L76            31 S L29 NOT L75
L77            31 S L76 AND L29-L75

     FILE 'WPIX' ENTERED AT 07:14:02 ON 26 MAR 2003
L78             3 S L29/BIX
L79             1 S L78 AND COATED MEMBRANE
L80         14656 S C12M/IC,ICM,ICS
L81            68 S L80 AND (L39/BIX OR L40/BIX OR L41/BIX OR L42/BIX OR L43/BIX
L82            57 S (R02038/DCN OR 2038/DRN) AND L80
L83            97 S L81,L82
L84            12 S L83 AND (POLYOL OR POLY OL OR POLYHYDRIC(L)ALCOHOL OR SUCROSE
L85           375 S L80 AND (B04-C03 OR C04-C03)/MC
L86           456 S L83,L85
L87            53 S L86 AND ((POLYOL OR POLY OL OR POLYHYDRIC(L)ALCOHOL OR SUCROS
L88             7 S L86 AND (B07-A02B OR C07-A02B OR B07-A02 OR C07-A02)/MC
L89            58 S L87,L88
L90             2 S L89 AND (0418/DRN OR R00418/DCN OR (TROMETHAMINE OR TRIS HYDR
L91             2 S L89 AND (B10-B03? OR C10-B03?)/MC
L92           215 S (B11-C08C OR C11-C08C)/MC AND L80
L93          4229 S (M424 OR M740)/M0,M1,M2,M3,M4,M5,M6 AND L80
L94           312 S L92,L93 AND L86
L95            40 S L94 AND L89
L96            15 S L95 AND ?MEMBRAN?/BIX
L97             2 S L90,L91 AND L95
L98             2 S L79,L97
L99             1 S L98 NOT FOLDING/TI
L100           14 S L96 NOT L98
L101           38 S L95 NOT L98
L102            7 S L100,L101 AND C12N005/IC,ICM,ICS,ICA,ICI
L103           34 S L100,L101 AND (D05-H08/MC OR (N136 OR Q233)/M0,M1,M2,M3,M4,M5
L104           11 S L100,L101 AND D05-H10/MC
L105           15 S L102,L104
L106            8 S L99,L102
L107            8 S L105 NOT L106
L108            8 S L106 AND L78-L107
L109            8 S L107 AND L78-L108

     FILE 'WPIX' ENTERED AT 07:50:55 ON 26 MAR 2003

     FILE 'DPCI' ENTERED AT 07:51:24 ON 26 MAR 2003
               E EP1195432/PN
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